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# CHEMICAL-QUANTUM STUDY OF RUTIN ACTIVITY AS A POSSIBLE TREATMENT FOR COVID-19.

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## ABSTRACT

Rutin, also called rutoside, quercetin-3-rutinoside and soforin, is the glucoside between the flavonol quercetin and the disaccharide rutinose. It is a dietary flavonoid widely distributed in vegetables and fruits; it has many therapeutic properties, mainly attributed to its powerful antioxidant and anti-inflammatory activities; its absorption can be influenced by its quantity and bioavailability. This research aimed to study the interactions of rutin and sars-cov-2 spike proteins as a possible treatment for the covid-19 disease. It used the Hamiltonian combinatorial possibilities to perform all the valence electron's hops between each substance. It used HC Semi-Empirical Parameterized Model number 3 (SE-PM3) to draw the corresponding molecules. Then it selected SE-PM3. It optimized the geometry with the Polak Ribiere method and calculated the variables of HOMO-LUMO, BG, EP, and other properties, resulting in a Tab-delimited table for BG and EP. The characterization results of the sars-cov-2 spike show that the amino acid (AA) Leu is presented as the most amount of all the amino acid sequencing of the sars-cov-2 spike. In contrast, the AA with the least amount in the sequencing is tryptophan. Here, rutin is an oxidizing agent of all the amino acids that make up the sars-cov-2 proteins. This means that the rutin can neutralize and even destroy sars-cov-2.

**KEYWORD:** Rutin, quantum chemistry, sars-cov-2, covid-19, HOMO, LUMO.

## INTRODUCTION

### Rutin

Rutin, also called rutoside, quercetin-3-rutinoside and soforin, is the glucoside between the flavonol quercetin and the disaccharide rutinose. It is formed by creating a bond between the disaccharide and the hydroxyl group of quercetin.[1] It is a dietary flavonoid widely distributed in vegetables and fruits; it has many therapeutic properties, mainly attributed to its powerful antioxidant and anti-inflammatory activities, its absorption can be influenced by its quantity and bioavailability.[2]

It is a flavonoid of nutritional importance, and it belongs to one of the best classes of natural antioxidants. It has antiprotozoal, antibacterial, and antiviral properties.[3] Its name comes from the Ruta graveolens plant, and chemically it is a glycoside that comprises flavonols aglycone quercetin and the disaccharide rutinose.[4] Other of its functions are the elimination of DPPH radicals and the inhibition of lipid peroxidation.[5]

### Rutin and its relationship with SARS-CoV-2 and COVID-19

Rutin has the highest interaction score with COVID-19 among all phytochemicals; it is proven that the ligand-protein interaction contacts' analysis reveals three residues (Glu166, Gly143, and Thr45) of the primary protease form bonds of hydrogen with the grind. It is also an effective inhibitor of several COVID-19 protein targets, including the significant protease and other critical proteins in the COVID-19 life cycle.[6]

The antimicrobial potential of rutin is demonstrated in the inhibition of essential SARS-CoV-2 proteins, including significant protease (Mpro), RNA-dependent RNA polymerase (RdRp), papain-like protease (PLpro), and protein peak (S), in all proteins shows a high grade. [7] It also inhibits platelet aggregation, as well as decreases vascular permeability, making the blood less thick and improving circulation.

### SARS-CoV-2

Belongs to the family of β-coronaviruses, single-stranded ribonucleic acid (RNA) viruses, positive polarity, enveloped, not segmented, with a genome of 27 to 32 kb and a size of 80-160 nm. The SARS-CoV-2 genome has 96% homology with a beta-coronavirus described in bats and 91% with a pangolin beta-coronavirus; hence it is considered the definitive host (origin) and intermediary.

There are asymptomatic carriers capable of transmitting the virus and even developing lung lesions demonstrated by imaging despite not presenting any clinical manifestation. Similarly, presymptomatic transmission is possible, that is, during the incubation period, this is a factor key for the transmission of SARS-CoV-2 given the high viral excretion in the upper respiratory tract, even in presymptomatic patients.

SARS-CoV-2 infection, with a sizeable viral load in the body, destroys human lungs through cytokine storms, especially in the elderly and people with immunosuppressed disorders. Phylogenetic analysis of the genomes suggests that the possible occurrence of recombination between pangolin and bat SARS-like CoVs could have led to the origin of SARS-CoV-2 and the COVID-19 outbreak.[8]

The SARS-CoV-2 infection is a zoonosis, the transmission routes between humans are similar to those described for other coronaviruses, the main one being by direct contact through the inhalation of respiratory drops and aerosols emitted by a sick person (respiratory drops more significant than 5 microns that can be transmitted up to 2 meters away).[9-10]

## COVID-19

The onset of COVID-19 manifests mainly as fever, but sometimes only chills and respiratory symptoms occur due to mild dry cough and gradual dyspnea and fatigue, and even diarrhea. Other persistent symptoms, according to the World Health Organization (WHO), are expectoration (33%), odynophagia (14%), headache (14%), myalgia or arthralgia (15%), nausea or vomiting (5%), nasal congestion (5%). In 80% of COVID-19 cases, the disease is mild, to the point of being confused with flu or colds. However, 15% of patients show severe symptoms that require hospitalization, and 5% develop severe symptoms that must be treated in intensive care units. Early detection of asymptomatic patients is of utmost importance because the clinical picture may have an unexpected torpid evolution and lead the patient to death. Even if they have a low viral load that does not represent an imminent danger to their life, it must be evaluated accordingly.[11]

## MATERIALS AND METHODS

### A. Hamiltonian technic

It used, the Hamiltonian combinatorial possibilities to perform, all the valence electron's hops between each of the substances.[12,13]

### B. Quantum Methodology

It bought the molecular simulator Hyper Chem (HC). (Hyper Chem. Hypercube, MultiON for Windows. Serial #12-800-1501800080. MultiON. Insurgentes Sur 1236 - 301 Tlacoquemecatl Col. del Valle, Delegación Benito Juárez, D. F., México CP. 03200).

It used, HC Semi-Empirical Parameterized Model number 3 (SE-PM3) to draw the corresponding molecules. Then it selected SE-PM3. It optimized the geometry with the Polak Ribiere method and, conducted the calculation of the variables of HOMO-LUMO, BG, EP and other properties, resulting in a Tab-delimited table for BG and EP.

The specific parameters selected for each of the simulations were as follows:
SET UP. Semi-emprical Method: PM3. Semi-Emprical Options: Charge and Spin. Total Charge 0. Spin Multiplicity 1. SCF Control. Converge limit 0.01. Interation limit 1000. Accelerate converge Yes. Spin Pairing Lowest. Overlap Weighting Factors Sigma-Sigma 1, Pi-Pi 1. Polarizabilities do not calculate.

COMPUTE 1. Geometry Optimization. Algorithm Polak Ribiere (conjugate gradient). Options Termination conditions. RMS gradient of 0.1 kcal/mol or 1000 maximun cycles. In vacuo yes. Screen refresh period 1 cyclos.

COMPUTE 2. Orbitals. Plot Orbital Options Isosurface Rendering. Orbital Contur Value 0.05. Rendering Wire mesh Isosurface Grid. Grid mesh size Coarse. Grid layout Default. Gird contour Default. Transparence level Default.

COMPUTE 3. Plot Molecular Graphs. Plot Molecular Options. Molecular Properties. Properties. Electrostatic Potential Yes. Representations. 3D Mapped Isosurface. Grid Mesh Size Coarse. Grid layout Default. Contour gird Default. Isosurface Rerending. Total Charge Density Contour Value (TCDCV) 0.015. Rendering Wire mesh. Transparence level Default. Mapped Options Functons Default.[14-20]

The characterization of the HER2 proteins was carried out with the Model6000 designed and published by the main author. The sequencing was taken from the NCBI website.[21]

## RESULTS AND DISCUTIONS

Table 1: shows the results of the characterization of the sars-cov-2 spike.

The AA Leu is presented as the statistical mode of all the AA sequencing of the sars-cov-2 spike. In contrast, the AA with the least amount in the sequencing is tryptophan.

**Table 1: Characterization of Sars-Cov-2 spike.**

| | AAs | | | Units | Percentage |
|---|---|---|---|---|---|
| 1 | a | A | Ala | 79 | 6.31% |
| 2 | r | R | Arg | 42 | 3.35% |
| 3 | n | N | Asn | 88 | 7.03% |
| 4 | d | D | Asp | 59 | 4.71% |
| 5 | c | C | Cys | 38 | 3.04% |
| 6 | q | Q | Gln | 62 | 4.95% |
| 7 | e | E | Glu | 46 | 3.67% |
| 8 | g | G | Gly | 81 | 6.47% |
| 9 | h | H | His | 16 | 1.28% |
| 10 | i | I | Ile | 76 | 6.07% |
| 11 | l | L | Leu | 106 | 8.47% |
| 12 | k | K | Lys | 58 | 4.63% |
| 13 | m | M | Met | 14 | 1.12% |
| 14 | f | F | Phe | 76 | 6.07% |
| 15 | p | P | Pro | 57 | 4.55% |
| 16 | s | S | Ser | 98 | 7.83% |
| 17 | t | T | Thr | 96 | 7.67% |
| 18 | w | W | Trp | 12 | 0.96% |
| 19 | y | Y | Tyr | 53 | 4.23% |
| 20 | v | V | Val | 95 | 7.59% |
| | | | Total | 1252 | 100.00% |

Table 2 presents the quantum well of the calculated ETCs values. In it, you can see that the rutin is at the bottom of the quantum well.

**Table 2: AAs and ordered substance in the quantum well.**

| No. | 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 | Arg | Arg | -9.176 | 0.558 | 9.734 | -0.165 | 0.199 | 0.364 | 26.742 |
| 1 | Rutin | Rutin | -7.629 | -0.566 | 7.062 | -0.120 | 0.232 | 0.352 | 20.064 |

Column 1 shows the sequential number of the ETCs of the quantum well. Column 2 demonstrates the reducing or antioxidant agent. Column 3 shows us the oxidizing agent. Columns 4,5, and 6 refer to the bandgap calculations. Columns 7, 8, and 9 are checked for the calculation of the electrostatic potential. Column ten specifies the calculation of the ETCs for each substance. It is observed that the rutin is at the bottom of the quantum well. Therefore, rutin is a more chemically stable substance than the 20 AAs of living beings. In this observation, it is concluded that rutin is a long-lived substance.

Table 3 shows oxide reduction interactions. It has the exact specifications as in table 2. Here, rutin is an oxidizing agent of all the AAs that make up the sars-cov-2 proteins. This means that the rutin can neutralize and even destroy sars-cov-2.

**Table 3: Oxide-reduction interactions. ETCs.**

| N | Reducing agent | Oxidizing agent | HOMO | LUMO | BG | E- | E+ | EP | ETC |
|---|---|---|---|---|---|---|---|---|---|
| 61 | Val | Val | -9.914 | 0.931 | 10.845 | -0.131 | 0.109 | 0.240 | 45.188 |
| *Reactions 22 to 60 are not shown in this table due to lack of space.* | | | | | | | | | |
| 21 | Ala | Rutin | -9.879 | -0.566 | 9.312 | -0.124 | 0.232 | 0.356 | 26.158 |
| 20 | Ile | Rutin | -9.872 | -0.566 | 9.306 | -0.128 | 0.232 | 0.360 | 25.849 |
| 19 | Rutin | Ser | -7.629 | 0.565 | 8.194 | -0.120 | 0.198 | 0.318 | 25.766 |
| 18 | Val | Rutin | -9.914 | -0.566 | 9.347 | -0.131 | 0.232 | 0.363 | 25.750 |
| 17 | Rutin | Arg | -7.629 | 0.558 | 8.187 | -0.120 | 0.199 | 0.319 | 25.664 |
| 16 | Leu | Rutin | -9.645 | -0.566 | 9.079 | -0.126 | 0.232 | 0.358 | 25.360 |
| 15 | Rutin | Tyr | -7.629 | 0.293 | 7.921 | -0.120 | 0.193 | 0.313 | 25.308 |
| 14 | Gly | Rutin | -9.902 | -0.566 | 9.336 | -0.137 | 0.232 | 0.369 | 25.301 |
| 13 | Rutin | Glu | -7.629 | 0.438 | 8.067 | -0.120 | 0.201 | 0.321 | 25.131 |
| 12 | Cys | Rutin | -9.639 | -0.566 | 9.072 | -0.129 | 0.232 | 0.361 | 25.131 |

| | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|
| 11 | Phe | Rutin | -9.553 | -0.566 | 8.987 | -0.126 | 0.232 | 0.358 | 25.102 |
| 10 | Lys | Rutin | -9.521 | -0.566 | 8.954 | -0.127 | 0.232 | 0.359 | 24.942 |
| 9 | Rutin | Met | -7.629 | 0.145 | 7.774 | -0.120 | 0.192 | 0.312 | 24.917 |
| 8 | Rutin | Asp | -7.629 | 0.420 | 8.049 | -0.120 | 0.204 | 0.324 | 24.843 |
| 7 | Pro | Rutin | -9.447 | -0.566 | 8.880 | -0.128 | 0.232 | 0.360 | 24.667 |
| 6 | Tyr | Rutin | -9.056 | -0.566 | 8.490 | -0.123 | 0.232 | 0.355 | 23.914 |
| 5 | Met | Rutin | -9.062 | -0.566 | 8.495 | -0.134 | 0.232 | 0.366 | 23.212 |
| 4 | Trp | Rutin | -8.299 | -0.566 | 7.732 | -0.112 | 0.232 | 0.344 | 22.477 |
| 3 | His | Rutin | -9.307 | -0.566 | 8.741 | -0.169 | 0.232 | 0.401 | 21.798 |
| 2 | Arg | Rutin | -9.176 | -0.566 | 8.610 | -0.165 | 0.232 | 0.397 | 21.687 |
| 1 | Rutin | Rutin | -7.629 | -0.566 | 7.062 | -0.120 | 0.232 | 0.352 | 20.064 |
| Statistical average | | | | | | | | | **29.158** |
| First quartile | | | | | | | | | **25.360** |

It is observed that all the oxidation-reduction interactions are conserved below the statistical average, while most of these interactions remain in the first quartile.

In table 4. We observe that rutin continues to oxidize the structural AAs of sars-cov-2 despite the multiple interactions.

**Table 4: Oxide-reduction interactions. All vs. all. Quantum soup.**

| **N** | **Reducing agent** | **Oxidizing agent** | **HOMO** | **LUMO** | **BG** | **E-** | **E+** | **EP** | **ETC** |
|---|---|---|---|---|---|---|---|---|---|
| **461** | Glu | Val | -10.374 | 0.931 | 11.305 | -0.111 | 0.109 | 0.220 | 51.388 |
| *Reactions 22 to 60 are not shown in this table due to lack of space.* | | | | | | | | | |
| **21** | Arg | Asp | -9.176 | 0.420 | 9.596 | -0.165 | 0.204 | 0.369 | 26.006 |
| **20** | Ile | Rutin | -9.872 | -0.566 | 9.306 | -0.128 | 0.232 | 0.360 | 25.849 |
| **19** | Rutin | Ser | -7.629 | 0.565 | 8.194 | -0.120 | 0.198 | 0.318 | 25.766 |
| **18** | Val | Rutin | -9.914 | -0.566 | 9.347 | -0.131 | 0.232 | 0.363 | 25.750 |
| **17** | Rutin | Arg | -7.629 | 0.558 | 8.187 | -0.120 | 0.199 | 0.319 | 25.664 |
| **16** | Leu | Rutin | -9.645 | -0.566 | 9.079 | -0.126 | 0.232 | 0.358 | 25.360 |
| **15** | Rutin | Tyr | -7.629 | 0.293 | 7.921 | -0.120 | 0.193 | 0.313 | 25.308 |
| **14** | Gly | Rutin | -9.902 | -0.566 | 9.336 | -0.137 | 0.232 | 0.369 | 25.301 |
| **13** | Rutin | Glu | -7.629 | 0.438 | 8.067 | -0.120 | 0.201 | 0.321 | 25.131 |
| **12** | Cys | Rutin | -9.639 | -0.566 | 9.072 | -0.129 | 0.232 | 0.361 | 25.131 |
| **11** | Phe | Rutin | -9.553 | -0.566 | 8.987 | -0.126 | 0.232 | 0.358 | 25.102 |
| **10** | Lys | Rutin | -9.521 | -0.566 | 8.954 | -0.127 | 0.232 | 0.359 | 24.942 |
| **9** | Rutin | Met | -7.629 | 0.145 | 7.774 | -0.120 | 0.192 | 0.312 | 24.917 |
| **8** | Rutin | Asp | -7.629 | 0.420 | 8.049 | -0.120 | 0.204 | 0.324 | 24.843 |
| **7** | Pro | Rutin | -9.447 | -0.566 | 8.880 | -0.128 | 0.232 | 0.360 | 24.667 |
| **6** | Tyr | Rutin | -9.056 | -0.566 | 8.490 | -0.123 | 0.232 | 0.355 | 23.914 |
| **5** | Met | Rutin | -9.062 | -0.566 | 8.495 | -0.134 | 0.232 | 0.366 | 23.212 |
| **4** | Trp | Rutin | -8.299 | -0.566 | 7.732 | -0.112 | 0.232 | 0.344 | 22.477 |
| **3** | His | Rutin | -9.307 | -0.566 | 8.741 | -0.169 | 0.232 | 0.401 | 21.798 |
| **2** | Arg | Rutin | -9.176 | -0.566 | 8.610 | -0.165 | 0.232 | 0.397 | 21.687 |
| **1** | Rutin | Rutin | -7.629 | -0.566 | 7.062 | -0.120 | 0.232 | 0.352 | 20.064 |

| | |
|---|---|
| Statistical average | **33.701** |
| Fisrst quartile | **30.594** |

## CONCLUSIONS

**We found out that**

1. Rutin is an oxidizing agent of all the AAs that make up the sars-cov-2 proteins.
2. Rutin is a long-lived substance.
3. Rutin can neutralize and even destroy Sars-Cov-2.
4. Rutin continues to oxidize the structural AAs of Sars-Cov-2 despite the multiple interactions that can occur.

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