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ANALYSIS OF QUANTUM-CHEMICAL INTERACTIONS OF FOLIC ACID AND SARS-COV-2 PROTEINS AS CAUSERS OF COVID-19

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ABSTRACT

The adaptive immune system is important for the control of most viral infections. Currently, knowledge is available on the relationships between antigen-specific immune responses and sars-cov-2 infection. This research aimed to analyze the chemical-quantum interactions of Folic Acid (FAc) and the sars-cov-2 proteins as the cause of covid-19. Hyperchem software was used to carry out all simulations. The electron transfer coefficient theory (ETC) was used to calculate this coefficient to rank the interactions. 21 oxide-reduction quantum interactions are observed at the bottom of the quantum well. These interactions are of 20 pure amino acids (AAs) and FAc. The FAc has higher stability among all of them. Out of 441 possible interactions mixed with AAs vs. FAc, 21 oxidant interactions and 7 antioxidant interactions were found at the bottom of the quantum well. With this finding, it is concluded that FAc can render the aars-cov-2 proteins useless and cause the inactivation or death of this coronavirus. Furthermore, FAc is known to strengthen the immune system.

KEYWORDS: Quantum-chemistry, folic acid, sars-cov-2, covid-19, electron transfer coefficient.

INTRODUCTION

The adaptive immune system is important for the control of most viral infections.[1,2] Currently, knowledge is available on the relationships between antigen-specific immune responses and sars-cov-2 infection.[3] A new concept has emerged among researchers that reveal that CD4 + T cells, CD8 + T cells.[4-7] Neutralizing antibodies are also known to contribute to the control of sars-cov2 in covid-19 cases. On the other hand, the specific functions and kinetics of these adaptive immune responses and the interaction with innate immunity, and the implications for covid-19 vaccines are discussed.[8-14]

Some researchers have examined a safe and cheap alternative against this virus by detecting hundreds of nutraceutical compounds against known therapeutic targets of sars-cov-2 by molecular coupling. The virtual scan results were then analyzed for binding energy and interactive residues and compared to some already known hits in the best binding pose. This study's analyses strongly predicted the potential of FAc and its derivatives, such as tetrahydro folic acid and 5-methyl tetrahydro folic acid against sars-cov-2. The strong and stable binding affinity of this water-soluble vitamin and its derivatives against sars-cov-2 indicates that they could be valuable drugs against the management of this covid-19 pandemic. This study could serve as a starting point for further investigating these molecules through in vitro and in vivo assays.[15-20]

In contrast, other researchers do not agree with the use of nutraceutical substances to treat or prevent covid-19. These tell us that the scientific justification for the use of FAc as a placebo in covid-19 trials seems scientifically unbelievable, and this may be a major factor in the failure of many agents. We must be more careful when choosing our placebo, especially when conducting a placebo-controlled trial.[21] Quantum chemistry has been little valued and used by scientists; however, the calculations made by this methodology are close to reality. We calculate these interactions using computer simulations. Another tool we used was the electron transfer coefficient theory (published by Dr. Manuel González Pérez in 2017). Seeing the controversies between some researchers, we set the objective of this research "to analyze the chemical-quantum interactions of FAc and sars-cov-2 proteins as the cause of covid-19."

MATERIAL AND METHODS

Hyperchem software was used to carry out all simulations. The ETC theory was used to calculate this coefficient to rank the interactions.[22]

Below are the specific parameter tables.

Table 1 shows the general parameters of the simulator. For energy minimization, the Polak-Rebiere model was used.

Table 1: Parameters used for quantum computing molecular orbitals HUMO and LUMO.

Parameter	Value	Parameter	Value
Total charge	0	Polarizability	Not
Spin Multiplicity	1	Geometry Optimization algorithm	Polak-Ribiere (Conjugate Gradient)
Spin Pairing	RHF	Termination condition RMS gradient of	0.1 Kcal/Amol
State Lowest Convergent Limit	0.01	Termination condition or	1000 maximum cycles
Interaction Limit	50	Termination condition or	In vacuo
Accelerate Convergence	Yes	Screen refresh period	1 cycle

In table 2. We use the parameter 0.015 to measure the surfaces of the molecules. In previous articles, this parameter was used to standardize the calculations.[23-26]

Table 2: Parameters used for visualizing the map of the electrostatic potential of the molecules.

Parameter	Value	Parameter	Value
Molecular Property	Property Electrostatic Potential	Contour Grid increment	0.05
Representation	3D Mapped Isosurface	Mapped Function Options	Default
Isosurface Grid: Grid Mesh Size	Coarse	Transparency level	A criteria
Isosurface Grid: Grid Layout	Default	Isosurface Rendering: Total charge density contour value	0.015
Contour Grid: Starting Value	Default	Rendering Wire Mesh	

The ETC is the parameter that helps us to rank and compare all interactions.[22]

$ETC = \frac{|BG|}{EP}$ Equation 1

Where:

BG = Band Ban (acronym in English)

EP = Electrostatic potential.

ETC = Electron Transfer Coefficient.

Each table is a summary of these calculations.

We obtained the calculations of each of the orbitals and electrostatic potentials of the FAc. Figure 1 shows us the molecular images of the calculations that were used in each of the tables.

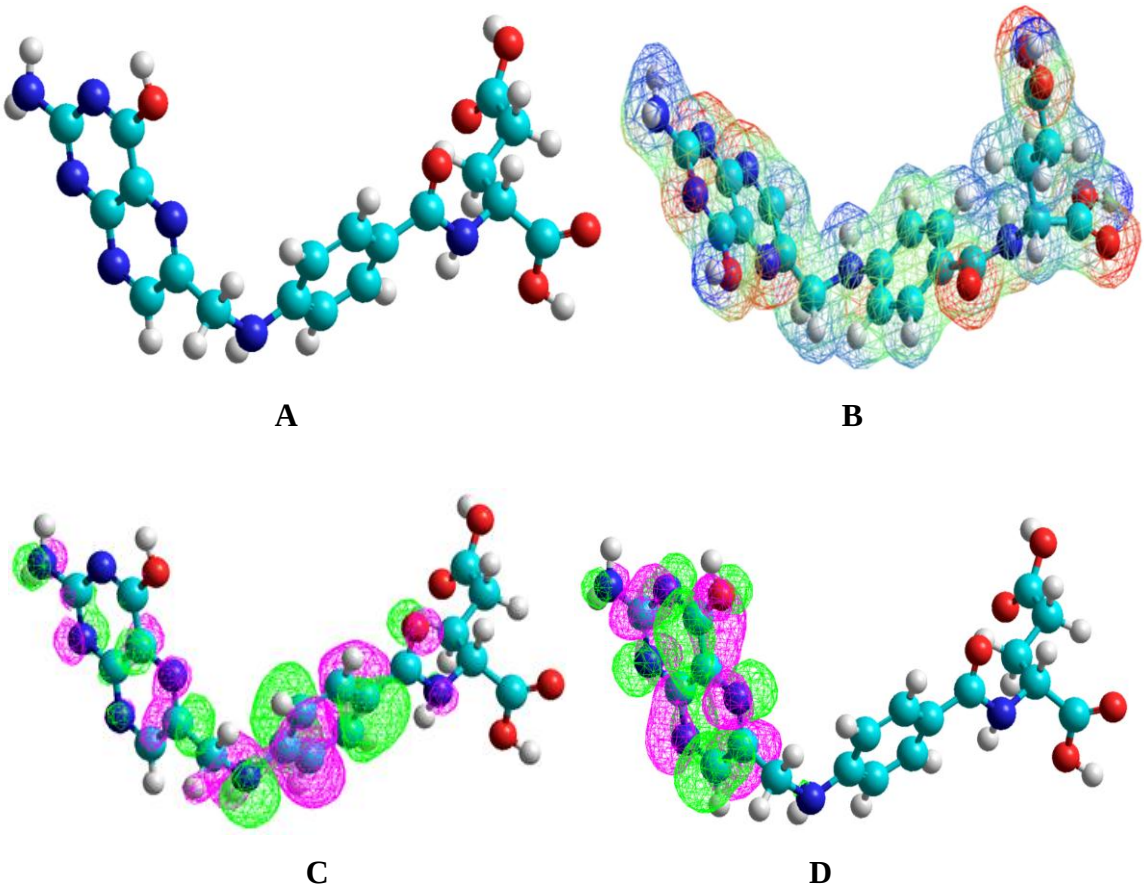

Figure 1: C = Cyan, N = Blue, H = White, O = Red. A) FAc molecule; B) Electrostatic potential of FAc; C) Orbital of valence HOMO; D) Orbital of valence LUMO.

Table 3 shows 7 sars-cov-2 proteins. These proteins were cleared out of 20 in total. The Sars15 protein is a spike of the coronavirus; this protein is the largest of all. To get a better idea, it is more than ten times the size of insulin.[27-34]

Table 3: Summary of AA content for each component of sars-cov-2.

AAs	Sars6	Sars7	Sars11	Sars13	Sars15	Sars18	Sars19
Ala	9	2	12	12	81	17	8
Arg	3	1	11	9	42	11	11
Asn	14	5	21	17	88	21	8
Asp	9	3	9	12	61	17	6
Cys	0	0	9	8	30	12	0
Gln	10	2	7	6	66	14	6
Glu	6	4	7	6	51	9	4
Gly	13	1	15	15	94	26	17
His	0	0	1	0	26	7	1
Ile	10	5	9	8	71	11	5
Leu	17	5	14	14	107	29	7
Lys	8	2	12	12	58	11	6
Met	0	0	0	1	11	10	1
Phe	2	0	16	16	79	17	3
Pro	1	0	13	13	63	13	9
Ser	14	3	17	16	105	16	7
Thr	3	0	13	14	95	24	9
Trp	0	0	2	2	12	3	3
Tyr	2	0	15	15	53	11	6
Val	11	3	20	21	95	27	2
Total	132	36	223	217	1288	306	119
The sequencing of these proteins was taken from the NCBI and quantified with a program designed by us called "Modelo6000".							

It is observed that the peak protein Sars15 has Leu as a statistical mode parameter, as do most of the glucose transporters GLUT and SGTL. Simultaneously, the protein Sars19 (partial nucleocapsid phosphoprotein, which causes severe acute respiratory syndrome) has Gly, as does collagen, as a statistical mode.

Table 4: Meaning of the columns of table 3.

Sars6	Chain F, 2019-nCoV S2 subunit,2019-nCoV S2 subunit
Sars7	Chain A, 2019-nCoV S2 subunit
Sars11	Chain F, 2019-nCoV Receptor Binding Domain
Sars13	Chain F, 2019-nCoV chimeric RBD
Sars15	Chain C, Spike glycoprotein
Sars18	Chain A, Non-structural polyprotein 1ab
Sars19	nucleocapsid phosphoprotein, partial [Severe acute respiratory syndrome coronavirus 2]

Continuing with the analysis, in table 5, column 1 represents the location number in the quantum well. The numbering goes according to the number line. In column 2, the reducing agents are presented. These give up electrons. In column 3, the oxidizing agents are

represented. These accept electrons. Columns 4, 5, and 6 represent the valence molecular orbital calculations for each molecule. Colons 7, 8, and 9 represent all calculations of the electrostatic potentials for each molecule. Column 10 represents the calculation of the electron transfer coefficient.

It is also observed that the FAc is at the bottom of the quantum well. This position is interpreted as the most stable chemical of all those presented in this table. If FAc is the most stable of all, this leads us to conclude that FAc is complicated to eliminate from biological systems.

Table 5: ETCs of pure AAs and FAc ordered in the quantum well.

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	Arg	Arg	-9.176	0.558	9.734	-0.165	0.199	0.364	26.742
1	*FAc	*FAc	-9.017	-1.335	7.681	-0.119	0.194	0.313	24.541
* *FAc is the most stable substance among all AAs in living beings.*									

Table 6 shows 21 oxide-reduction quantum interactions at the bottom of the quantum well out of 61 in total. These interactions are the most stable ones oxidized by FAC to various AAs of the sars-cov-2 proteins. Even the probability that they will destroy or disable the sars-cov-2 proteins is exceedingly high, and robust.

Table 6: Bottom of the quantum well of oxide-reduction interactions.

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
40 interactions are skipped for reasons of space.									
21	His	His	-9.307	0.503	9.811	-0.169	0.171	0.340	28.855
20	Met	Met	-9.062	0.145	9.207	-0.134	0.192	0.326	28.243
19	Gln	FAc	-10.023	-1.335	8.688	-0.124	0.194	0.318	27.320
18	Thr	FAc	-9.896	-1.335	8.561	-0.123	0.194	0.317	27.006
17	Asn	FAc	-9.929	-1.335	8.594	-0.125	0.194	0.319	26.939
16	Ala	FAc	-9.879	-1.335	8.543	-0.124	0.194	0.318	26.866
15	Arg	Arg	-9.176	0.558	9.734	-0.165	0.199	0.364	26.742
14	Ile	FAc	-9.872	-1.335	8.537	-0.128	0.194	0.322	26.511
13	Val	FAc	-9.914	-1.335	8.578	-0.131	0.194	0.325	26.395
12	Leu	FAc	-9.645	-1.335	8.310	-0.126	0.194	0.320	25.968
11	Gly	FAc	-9.902	-1.335	8.567	-0.137	0.194	0.331	25.882
10	Cys	FAc	-9.639	-1.335	8.303	-0.129	0.194	0.323	25.707
9	Phe	FAc	-9.553	-1.335	8.218	-0.126	0.194	0.320	25.680
8	Lys	FAc	-9.521	-1.335	8.185	-0.127	0.194	0.321	25.499
7	Pro	FAc	-9.447	-1.335	8.111	-0.128	0.194	0.322	25.189
6	FAc	FAc	-9.017	-1.335	7.681	-0.119	0.194	0.313	24.541
5	Tyr	FAc	-9.056	-1.335	7.721	-0.123	0.194	0.317	24.355
4	Met	FAc	-9.062	-1.335	7.726	-0.134	0.194	0.328	23.556
3	Trp	FAc	-8.299	-1.335	6.963	-0.112	0.194	0.306	22.755
2	His	FAc	-9.307	-1.335	7.972	-0.169	0.194	0.363	21.961
1	Arg	FAc	-9.176	-1.335	7.841	-0.165	0.194	0.359	21.841

Certainly, these interactions take place with many human proteins; but humans have metabolic mechanisms to take advantage of them by strengthening our immune system.
In other words, human beings benefit from these interactions; but for sars-cov-2, they can be fatal.

Table 7 shows a soup of quantum interactions "all against all", 441 of them are omitted for reasons of space. Here, the FAc follows the same oxidation pattern as the AAs of the sars-cov-2 proteins.

The five strongest and most probable interactions lie at the bottom of the quantum well. Arg-FAc is the most likely, followed by His-FAc, Trp-FAc, Met-FAc, Tyr-FAc.

Table 7: Quantum soup. All against all.

N	Reducing Agent	Oxidizing Agent	HOMO	LUMO	BG	E-	E+	EP	ETC
441	Glu	Val	-10.374	0.931	11.305	-0.111	0.109	0.220	51.388
420 interactions are skipped for reasons of space .									
21	Ile	FAc	-9.872	-1.335	8.537	-0.128	0.194	0.322	26.511
20	Arg	Tyr	-9.176	0.293	9.469	-0.165	0.193	0.358	26.449
19	Val	FAc	-9.914	-1.335	8.578	-0.131	0.194	0.325	26.395
18	His	Glu	-9.307	0.438	9.746	-0.169	0.201	0.370	26.340
17	Arg	Glu	-9.176	0.438	9.615	-0.165	0.201	0.366	26.269
16	His	Met	-9.307	0.145	9.453	-0.169	0.192	0.361	26.184
15	Arg	Met	-9.176	0.145	9.321	-0.165	0.192	0.357	26.110
14	His	Asp	-9.307	0.420	9.728	-0.169	0.204	0.373	26.079
13	Arg	Asp	-9.176	0.420	9.596	-0.165	0.204	0.369	26.006
12	Leu	FAc	-9.645	-1.335	8.310	-0.126	0.194	0.320	25.968
11	Gly	FAc	-9.902	-1.335	8.567	-0.137	0.194	0.331	25.882
10	Cys	FAc	-9.639	-1.335	8.303	-0.129	0.194	0.323	25.707
9	Phe	FAc	-9.553	-1.335	8.218	-0.126	0.194	0.320	25.680
8	Lys	FAc	-9.521	-1.335	8.185	-0.127	0.194	0.321	25.499
7	Pro	FAc	-9.447	-1.335	8.111	-0.128	0.194	0.322	25.189
6	FAc	FAc	-9.017	-1.335	7.681	-0.119	0.194	0.313	24.541
5	Tyr	FAc	-9.056	-1.335	7.721	-0.123	0.194	0.317	24.355
4	Met	FAc	-9.062	-1.335	7.726	-0.134	0.194	0.328	23.556
3	Trp	FAc	-8.299	-1.335	6.963	-0.112	0.194	0.306	22.755
2	His	FAc	-9.307	-1.335	7.972	-0.169	0.194	0.363	21.961
1	Arg	FAc	-9.176	-1.335	7.841	-0.165	0.194	0.359	21.841

Table 8 summarizes the calculations for each quartile of the general quantum well. There are 7 antioxidant interactions and 21 oxidant interactions, 28 probable and powerful interactions between the AAs of the sars-cov-2 proteins and the FAc.[27-34]

Table 8: Summary of all the molecular interactions of the AAs of the sars-cov-2 proteins and the FAc.

Quartile 1		Quartile 2		Quartile 3		Quartile 4	
RA	OA	RA	OA	RA	OA	RA	OA
7	21	7	0	3	0	4	0
The first quartile has 28 possible molecular interactions from the interaction of FAc with the AAs of sars-cov-2.							

For clarity, the quantum well with its quartiles is drawn in figure 2.

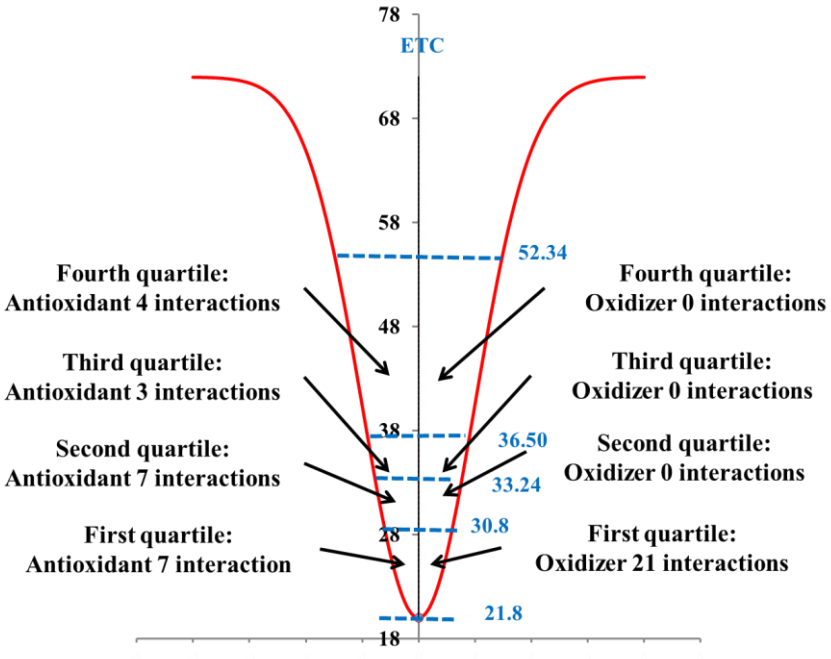

Figure 2: Schematic of the quantum well and its quartiles. It is observed that the first quartile has 7 antioxidant interactions and 21 oxidant interactions, a total of 28. In the first quartile, the interactions are stronger and more probable.

CONCLUSIONS

1. We made the characterization of the AAs of the sars-cov-2 proteins. Its spike was found to have the Leu as a statistical mode. Insulin has the same AA as a statistical mode—table 3.
2. We calculate the interactions of the 20 pure AAs of sars-cov-2 and FAc. It is concluded that the FAc is more stable than all AAs. Table 5.
3. The oxidation-reduction quantum interactions of FAc vs. all AAs of the sars-cov-2 proteins and these interactions occur at the bottom of the quantum well table 6.
4. With these interactions, it was possible to predict that Fac is highly interactive with all AAs of the sars-cov-2 proteins.
5. We calculate the ETCs "all against all" in table 7, and we observe the same pattern as table 6.
6. Table 8 presents a summary of all the interactions of the FAc vs. AAs from sars-cov-2. Besides, it is represented by a drawing of the quantum well.

As a general conclusion, we say that the AcF can interact with the AAs of the sars-cov-2 proteins. This interaction can disable or destroy sars-cov-2. Human proteins have the same probability of interaction, but it has metabolized FAc for millions of years. Even in the

scientific literature, many benefits of FAc for human health are enunciated. One of these benefits is the strengthening of the immune system.[35-37]

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