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QUANTIC CHEMICAL ANALYSIS OF THE INTERACTION OF CORTISONE, INSULIN AND GLUCOSE

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ABSTRACT

In recent years, doctors have linked the dosage of Cortisone (CTS) as a cause of hyperglycemia in patients. The objective of this research is to study the interaction of glucose, insulin, and as a cause of hyperglycemia in humans. The hyperchem quantum simulator and specifically the Semi-Empirical Parametric Method 3 (SE-PM3) will be used. The values of the electronic transfer coefficients of glucose, Cor and insulin with their corresponding amino acids will be calculated. It is expected to determine the interaction between the active sites of insulin and its interaction with glucose and CTS. In conclusion, we hope to verify the theoretical hypothesis that CTS is responsible for hyperglycemia in humans.

KEYWORDS: Cortisone, Insulin, Glucose, Quantum Chemical, SE-PM3.

INTRODUCTION

The cortisone

CTS is a hormone from the group of lipids and belongs to steroids.[1] This hormone is used in the form of injections, orally and in the form of creams;[11] it is used as a medication to relieve transient joint pain.[2] Doctors can prescribe CTS to prevent allergic reactions, arthritis, ulcerative colitis, polymyalgia rheumatic, and skin diseases.[3-5] In rare cases, CTS is used to treat some types of cancer.[6]

CTS produces reasonably uncomfortable short-term side effects. These effects are insomnia, fluid retention, and change in blood sugar levels, headache, burning and bad mood.[7] On the other hand, when CTS is consumed, long-term effects appear that can be irreversible. These effects produce diabetes, high blood pressure, bone diseases, high fatigue, bloody stools, and vomiting. One of these most dangerous effects is the impact on the growth of children.[8] When the patient takes synthetic CTS for a long time, it acquires a physical and psychological dependence.[9]

The insulin

Insulin decreases blood glucose concentration. It increases cell permeability to monosaccharides, amino acids and fatty acids. It accelerates glycolysis, the pentose phosphate cycle, and glycogen synthesis in liver.[10]

The glucose and diabetes

Diabetes and high blood glucose have been associated with many parallel diseases.[11] Researchers around the world have associated too the hyperglycemia with the supply of CTS in the patients.[12-14]

The objective of this article is to show that the supply of CTS causes hyperglycemia.

MATERIALS AND METHODS

We searched PubChem for the CTS molecule (figure 1); with this molecule, we made the quantum calculations of the ETC of the CTS. For these calculations, we use Hypercube Hyperchem software.

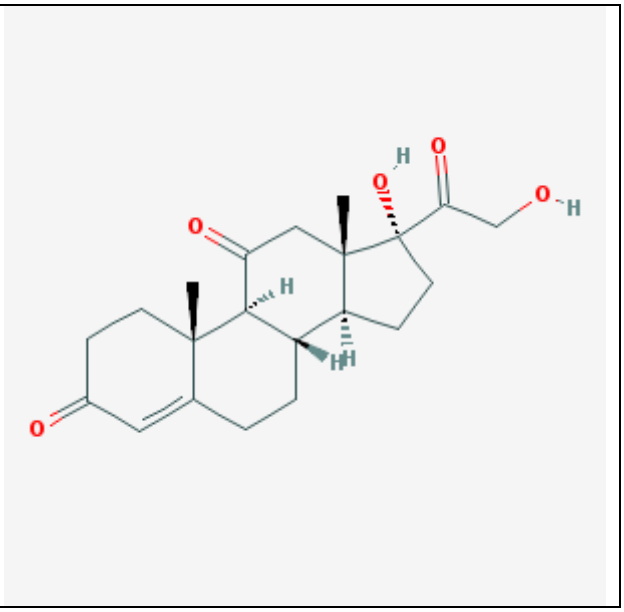
PubChem CID: 222786 Chemical Names: Cortisone; 53-06-5; Andreson; Cortisal; Cortisate; Cortistal Molecular Formula: C21H28O5 Molecular Weight: 360.45 g/mol InChI Key: MFYSYFVPBJMHGN-ZPOLXVRWSA-N Drug Information: Clinical Trials FDA Orange Book FDA UNII	

Figure 1. Classification and structure of CTS. PubChem.

We also use the database of the National Center for Biotechnology Information (NCBI)[15] and the Model 6000[16] to characterize insulin.

The quantum theory and the appropriate quantum methods were used and previously published by our project manager.[17-22]

RESULTS AND DISCUSSIONS

In Table 1, the characterization of human insulin P01380.1 is shown. The amino acid Leu is the most abundant in the entire polypeptide chain.[23]

Table 1. RecName: Full=Insulin; Contains: RecName: Full=Insulin B chain; Contains: RecName: Full=Insulin A chain; Flags: Precursor. UniProtKB/Swiss-Prot: P01308.1. Amino acid content of the homo sapiens insulin. Sequencing data taken from the NCBI.

N	AA			Quantity	Percentage
1	a	A	Ala	10	9.09%
2	r	R	Arg	5	4.55%
3	n	N	Asn	3	2.73%
4	d	D	Asp	2	1.82%
5	c	C	Cys	6	5.45%
6	q	Q	Gln	7	6.36%
7	e	E	Glu	8	7.27%
8	g	G	Gly	12	10.91%
9	h	H	His	2	1.82%
10	i	I	Ile	2	1.82%
11	l	L	Leu	20	18.18%

12	k	K	Lys	2	1.82%
13	m	M	Met	2	1.82%
14	f	F	Phe	3	2.73%
15	p	P	Pro	6	5.45%
16	s	S	Ser	5	4.55%
17	t	T	Thr	3	2.73%
18	w	W	Trp	2	1.82%
19	y	Y	Tyr	4	3.64%
20	v	V	Val	6	5.45%
			Total	110	100.00%
LOCUS INS_HUMAN 110 aa linear PRI 25-APR-2018 DEFINITION RecName: Full=Insulin; Contains: RecName: Full=Insulin B chain; Contains: RecName: Full=Insulin A chain; Flags: Precursor. ACCESSION P01308 VERSION P01308.1					

In Table 2, we can see that CTS has an intermediate ETC (interaction 9); this means that CTS can attack amino acids as an oxidizing agent or reducing agent. On the other hand, valine presents the highest ETC of all the substances studied; this means that this amino acid is the least stable or most reactive. In contrast, arginine presents the lower ETC of all the substances studied; for this reason, this amino acid is the most stable.

Table 2: ETC of amino acids including CTS.[24]

No.	Reducing agent	Oxidizing agent	HOMO	LUMO	BG	E-	E+	EP	ETC
1	Val	Val	-9.914	0.931	10.845	-0.131	0.109	0.240	45.188
2	Ala	Ala	-9.879	0.749	10.628	-0.124	0.132	0.256	41.515
3	Leu	Leu	-9.645	0.922	10.567	-0.126	0.130	0.256	41.279
4	Phe	Phe	-9.553	0.283	9.836	-0.126	0.127	0.253	38.879
5	Gly	Gly	-9.902	0.902	10.804	-0.137	0.159	0.296	36.500
6	Ser	Ser	-10.156	0.565	10.721	-0.108	0.198	0.306	35.037
7	Cys	Cys	-9.639	-0.236	9.403	-0.129	0.140	0.269	34.956
8	Glu	Glu	-10.374	0.438	10.812	-0.111	0.201	0.312	34.655
9*	CTS*	CTS*	-10.125	-0.224	9.901	-0.109	0.177	0.286	34.620
10	Ile	Ile	-9.872	0.972	10.844	-0.128	0.188	0.316	34.316
11	Thr	Thr	-9.896	0.832	10.728	-0.123	0.191	0.314	34.167
12	Gln	Gln	-10.023	0.755	10.778	-0.124	0.192	0.316	34.108
13	Asp	Asp	-10.370	0.420	10.790	-0.118	0.204	0.322	33.509
14	Asn	Asn	-9.929	0.644	10.573	-0.125	0.193	0.318	33.249
15	Lys	Lys	-9.521	0.943	10.463	-0.127	0.195	0.322	32.495
16	Pro	Pro	-9.447	0.792	10.238	-0.128	0.191	0.319	32.095
17	Trp	Trp	-8.299	0.133	8.431	-0.112	0.155	0.267	31.577
18	Tyr	Tyr	-9.056	0.293	9.349	-0.123	0.193	0.316	29.584

19	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
21	Arg	Arg	-9.176	0.558	9.734	-0.165	0.199	0.364	26.742
*ETC of CTS. The ETC of CTS is located in the middle part of the NT interactions. For this reason, CTS attacks NTs in both directions: oxidation and molecular reduction.									

In table 3, The interaction 41, Arg: CTS presents the lowest ETC of the whole table and therefore is most likely of all. In turn, CTS does not appear as an antioxidant due to its very high ETCs (interactions: 1-13, 17-20, and 22-24).

As a curious or particular case, CTS is oxidized by the amino acids Asp, Glu, and Met.

Table 3. Cross bands ETCs CTS vs. Amino acids.

No	Reducing agent	Oxidizing agent	HOMO	LUMO	BG	E-	E+	EP	ETC
1	CTS	Val	-10.125	0.931	11.056	-0.109	0.109	0.218	50.716
2	CTS	Leu	-10.125	0.922	11.047	-0.109	0.130	0.239	46.222
3	CTS	Ala	-10.125	0.749	10.874	-0.109	0.132	0.241	45.121
4	CTS	Phe	-10.125	0.283	10.408	-0.109	0.127	0.236	44.103
5	CTS	Gly	-10.125	0.902	11.027	-0.109	0.159	0.268	41.144
6	CTS	Cys	-10.125	-0.236	9.889	-0.109	0.140	0.249	39.716
7	CTS	Trp	-10.125	0.133	10.258	-0.109	0.155	0.264	38.854
8	CTS	His	-10.125	0.503	10.628	-0.109	0.171	0.280	37.957
9	CTS	Ile	-10.125	0.972	11.097	-0.109	0.188	0.297	37.362
10	CTS	Thr	-10.125	0.832	10.957	-0.109	0.191	0.300	36.523
11	CTS	Lys	-10.125	0.943	11.068	-0.109	0.195	0.304	36.407
12	CTS	Pro	-10.125	0.792	10.917	-0.109	0.191	0.300	36.390
13	CTS	Gln	-10.125	0.755	10.880	-0.109	0.192	0.301	36.146
14	CTS	Asn	-10.125	0.644	10.769	-0.109	0.193	0.302	35.659
15	Glu	CTS	-10.374	-0.224	10.151	-0.111	0.177	0.288	35.245
16	Ser	CTS	-10.156	-0.224	9.933	-0.108	0.177	0.285	34.852
17	CTS	Ser	-10.125	0.565	10.690	-0.109	0.198	0.307	34.820
18	CTS	Arg	-10.125	0.558	10.683	-0.109	0.199	0.308	34.685
19	CTS	CTS	-10.125	-0.224	9.901	-0.109	0.177	0.286	34.620
20	CTS	Tyr	-10.125	0.293	10.418	-0.109	0.193	0.302	34.495
21	Asp	CTS	-10.370	-0.224	10.146	-0.118	0.177	0.295	34.394
22	CTS	Met	-10.125	0.145	10.270	-0.109	0.192	0.301	34.120
23	CTS	Glu	-10.125	0.438	10.563	-0.109	0.201	0.310	34.075
24	CTS	Asp	-10.125	0.420	10.545	-0.109	0.204	0.313	33.690
25	Gln	*CTS	-10.023	-0.224	9.800	-0.124	0.177	0.301	32.556
26	Thr	*CTS	-9.896	-0.224	9.673	-0.123	0.177	0.300	32.243
27	Asn	*CTS	-9.929	-0.224	9.705	-0.125	0.177	0.302	32.137
28	Ala	*CTS	-9.879	-0.224	9.655	-0.124	0.177	0.301	32.077

29	Ile	*CTS	-9.872	-0.224	9.648	-0.128	0.177	0.305	31.634
30	Val	*CTS	-9.914	-0.224	9.690	-0.131	0.177	0.308	31.462
31	Leu	*CTS	-9.645	-0.224	9.422	-0.126	0.177	0.303	31.095
32	Gly	*CTS	-9.902	-0.224	9.679	-0.137	0.177	0.314	30.824
33	Phe	*CTS	-9.553	-0.224	9.329	-0.126	0.177	0.303	30.790
34	Cys	*CTS	-9.639	-0.224	9.415	-0.129	0.177	0.306	30.769
35	Lys	*CTS	-9.521	-0.224	9.297	-0.127	0.177	0.304	30.582
36	Pro	*CTS	-9.447	-0.224	9.223	-0.128	0.177	0.305	30.239
37	Tyr	*CTS	-9.056	-0.224	8.832	-0.123	0.177	0.300	29.441
38	Met	*CTS	-9.062	-0.224	8.838	-0.134	0.177	0.311	28.419
39	Trp	*CTS	-8.299	-0.224	8.075	-0.112	0.177	0.289	27.941
40	His	*CTS	-9.307	-0.224	9.084	-0.169	0.177	0.346	26.254
41	Arg	*CTS	-9.176	-0.224	8.953	-0.165	0.177	0.342	26.177
* CTS as an oxidizing agent with lower ETCs and therefore more likely to oxidize.									

In contrast, we can see that CTS oxidizes all amino acids (table 3 *); due to this phenomenon, hyperglycemia can be explained. The CTS encapsulates the insulin, therefore it cannot catch the glucose to take it to its cellular receptor.

We made the comparison of ETC vs. abundance (table 4), and we found that there is no mathematical pattern defined in this comparison. We do not see that the amino acid of greater abundance (Leu) is not the one with the highest affinity with CTS. In contrast, the highest affinity amino acid Arg has an abundance of 4.55%.

To understand the zones of probable interactions, we calculate and graph the quantum wells of the three interactions most related to the CTS.

Table 4. Comparisons ETC vs. abundance.

No	Reducing agent	Oxidizing agent	ETC	Abundance percentage
25	Gln	*CTS	32.556	6.36%
26	Thr	*CTS	32.243	2.73%
27	Asn	*CTS	32.137	2.73%
28	Ala	*CTS	32.077	9.09%
29	Ile	*CTS	31.634	1.82%
30	Val	*CTS	31.462	5.45%
31	Leu	*CTS	31.095	18.18%
32	Gly	*CTS	30.824	10.91%
33	Phe	*CTS	30.790	2.73%
34	Cys	*CTS	30.769	5.45%
35	Lys	*CTS	30.582	1.82%
36	Pro	*CTS	30.239	5.45%

37	Tyr	*CTS	29.441	3.64%
38	Met	*CTS	28.419	1.82%
39	Trp	*CTS	27.941	2.73%
40	His	*CTS	26.254	1.82%
41	Arg	*CTS	26.177	4.55%

To understand the areas of probable interactions, we calculate and graph the quantum wells of the three interactions most related to the CTS (figures 1, 2 and 3).

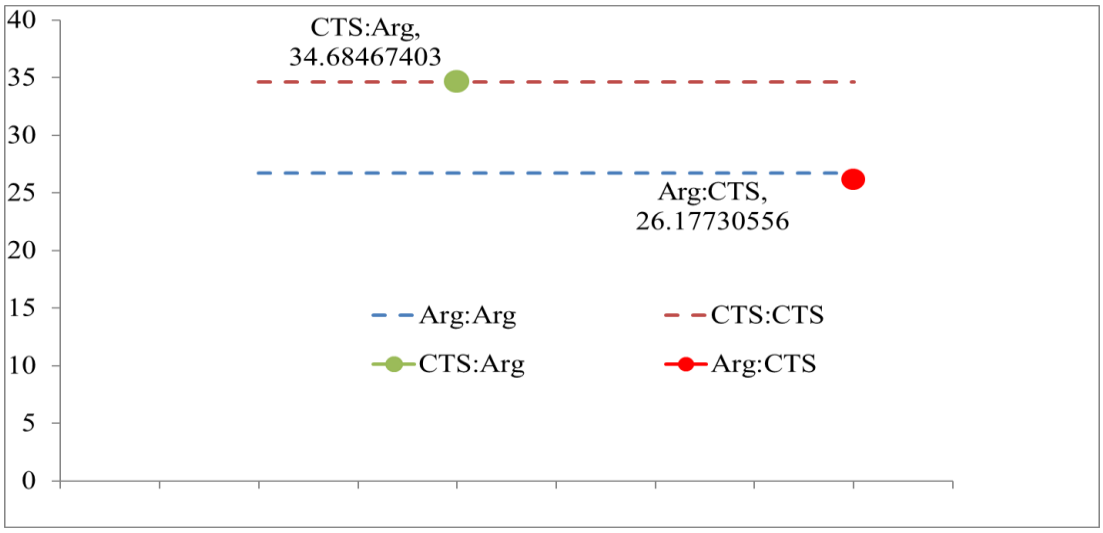


Figure 1. Quantum well of the cross-band interaction of the CTS: Arg.

We can observe two dotted lines that represent the bottoms of the quantum wells of the pure substances that are going to be combined.

We can observe two dotted lines that represent the bottoms of the quantum wells of the pure substances that are going to be combined.

The low probability zone is located above the red dotted line. The average probability zone is located between the two dotted lines. The high probability zone is located below the blue dotted line.

The red dot represents the bottom of the CTS cutaneous well as an oxidizing agent; while the green dot represents the bottom of the quantum well of the CTS as reducing agent or antioxidant.

The three figures conserve the same pattern, the CTS as an oxidizing agent in the most probable zone.

In this article, we do not graph the quantum wells of the 20 amino acids, but all the red dots fall in the same pattern; CTS as an oxidizing agent in the most likely area to interact.

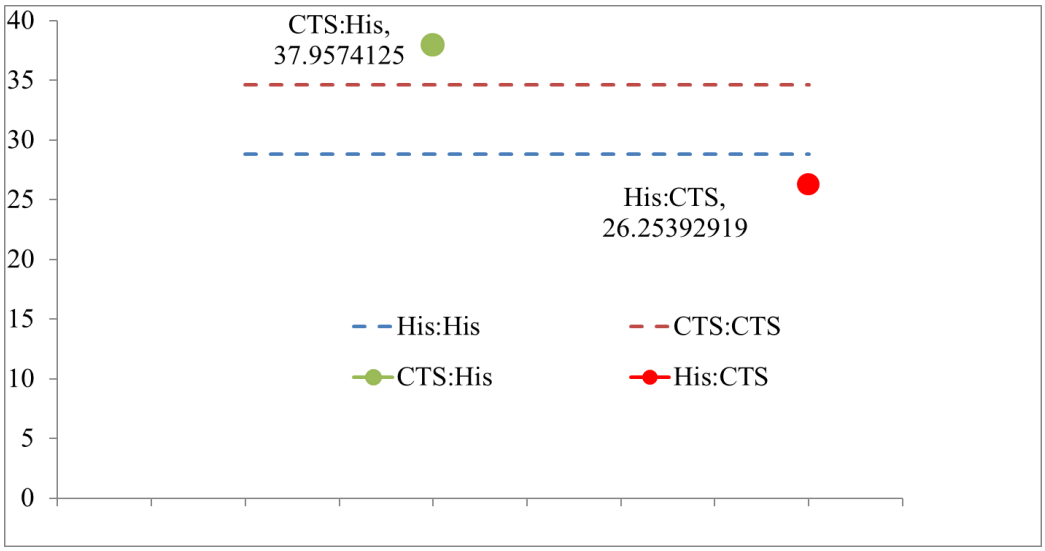


Figure 2. Quantum well of the cross-band interaction of the CTS:His.

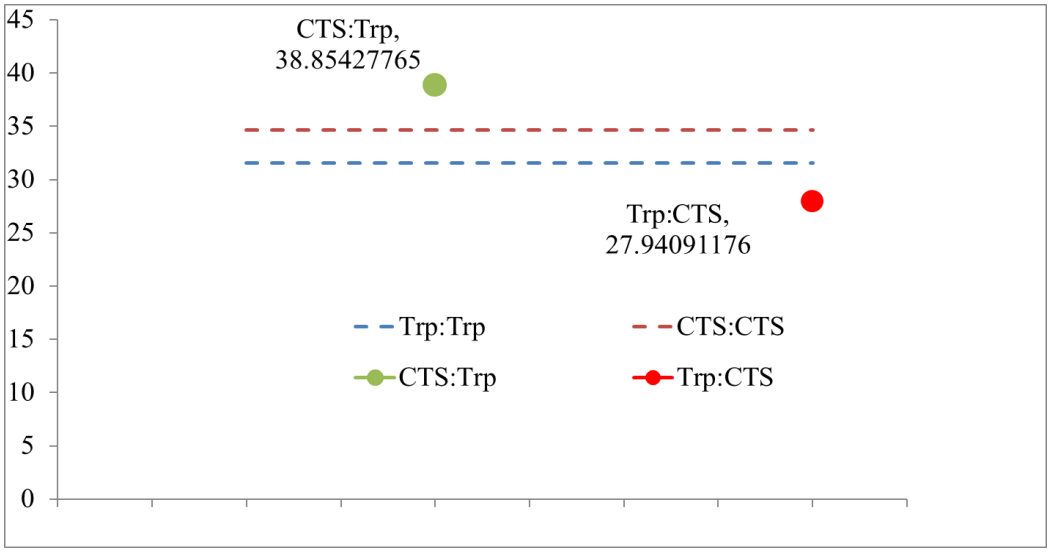


Figure 3. Quantum well of the cross-band interaction of the CTS:Trp.

CONCLUSIONS

We found that CTS encapsulates insulin and does not allow it to carry glucose to its cellular receptor. Because of this phenomenon, glucose is released into the bloodstream causing hyperglycemia.

Specifically, Arg is the amino acid that has the lowest ETC of all twenty amino acids present in insulin; therefore, this amino acid is the closest to interact with the CTS. However, Arg is not the most abundant amino acid in insulin. This observation leads us to conclude that the

abundance of amino acids in insulin and the stronger interaction with CTS do not present a mathematical pattern.

We demonstrate with the simulation of quantum chemistry that the excess of CTS in the human body is the cause of hyperglycemia.

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