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DIABETES: QUANTUM ANALYSIS OF THE INTERACTIONS OF CARNOSINE AND OTHER DIPEPTIDES VS. GLUCOSE

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ABSTRACT

The treatments with carnosine and other peptides have revolutionized science in recent years. Researchers show that treatment with carnosine improves glucose (GLU) metabolism, albuminuria, and pathology. The objective of this research was to analyze the chemical-quantum interactions of GLU with pure amino acids (AAs) and dipeptides. The hyperchem simulator was used to perform quantum calculations. These calculations are based on the Electron Transfer Coefficient (ETC). The following discoveries were made: the GLU is very aggressive and can attack any AA in its pure state. GLU also attacks dipeptides, polypeptides, and biological tissue. Carnosine has an ETC = 33.824, and there are other dipeptides with lower ETC. All dipeptides of Histidine (His) keep their ETC value = 33.824 constant, which is the ETC value of carnosine. It concluded that all dipeptides of His must have similar behavior to carnosine. Laboratory studies of these His dipeptides are suggested in order to control blood GLU and nephropathies for diabetic patients.

KEYWORDS: Diabetes, Quantum chemistry, Carnosine, Dipeptides, Glucose.

INTRODUCTION

The treatments with carnosine and other peptides[1-5] have revolutionized science in recent years. Researchers show that treatment with carnosine improves GLU metabolism, albuminuria, and pathology in mice. Therefore, carnosine could be a new therapeutic strategy to treat patients with Diabetic Nephropathy (DN) or be used to prevent DN in patients with diabetes.[6-10]

In other studies, carnosine, an endogenous dipeptide, showed significant recovery effects in the development of the neural tube. Higher expression levels of the Pax3 protein were found in the groups treated with carnosine. Also, the abnormal O-GlcNAcylation of the Pax3 protein was restored by carnosine. In this study, the molecular mechanisms of embryonic neurogenesis influenced by hyperglycemia were investigated using chicken embryo models. These results suggest new knowledge about the use of endogenous nutrients for the protection of the embryonic neurological development affected by the gestation of diabetes.[11] Another advantage of carnosine is that it can be a promising candidate to inhibit astrogliosis and promote the recovery of neurological function after ischemic stroke.[12]

On the other hand, the systemic and hepatic effects of the counterregulatory hormones and the glutamine dipeptide were investigated during episodes of hypoglycaemia, and it was found that during hepatic perfusion, gluconeogenesis was possibly the main route that led to the release of GLU.[13,14]

Arginine ($C_6H_{14}N_4O_2$) is nutritionally classified as a conditionally essential amino acid that can be commonly found in the protein component of plants and foods of animal origin. In the last two decades, studies have described its role as a mediator of multiple biological processes that include the release of various hormones, collagen synthesis during wound healing, antitumor activity, and immune cell responses. Typically, endogenous synthesis accounts for approximately 20% of daily expenditure, and normal levels of arginine in the blood range of 40 to 100 μmol / L, which can decrease by up to 20% in diabetes.[15]

The objective of this research was to analyze the chemical-quantum interactions of GLU with pure amino acids (AAs) and dipeptides.

METHODOLOGY

The hyperchem simulator was used to perform quantum calculations. These calculations are based on the Electron Transfer Coefficient (ETC) theory published in other articles. The same author also already published the database. In this database, it shows the ETCs of twenty AAs.[16-23]

RESULTS AND DISCUSSIONS

In Table 1 it can be seen that the GLU has a higher ETC than any of the AAs. Due to its high ETC, the GLU is very reactive with each of the AA.

On the other hand, it is observed that the Arg has the lowest ETC of the table; this tells us that this AA is the most stable of all.

Table 1: ETCs of 20 AAs and GLU.

No.	Reducing Agent	Oxidizing Agent	HOMO	LUMO	BG	E-	E+	EP	ETC
1	**GLU*	**GLU*	*-11.020*	*2.128*	*13.148*	*-0.116*	*0.169*	*0.285*	*46.135*
2	Val	Val	-9.914	0.931	10.845	-0.131	0.109	0.240	45.188
3	Ala	Ala	-9.879	0.749	10.628	-0.124	0.132	0.256	41.515
4	Leu	Leu	-9.645	0.922	10.567	-0.126	0.130	0.256	41.279
5	Phe	Phe	-9.553	0.283	9.836	-0.126	0.127	0.253	38.879
6	Gly	Gly	-9.902	0.902	10.804	-0.137	0.159	0.296	36.500
7	Ser	Ser	-10.156	0.565	10.721	-0.108	0.198	0.306	35.037
8	Cys	Cys	-9.639	-0.236	9.403	-0.129	0.140	0.269	34.956
9	Glu	Glu	-10.374	0.438	10.812	-0.111	0.201	0.312	34.655
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

Figures 1, 2 and 3 show the quantum wells of the specific interactions of AA and GLU. These three cross-band interactions between the GLU and the 20 AA are the lowest and fall in areas of highest probability from the quantum wells (probably very irreversible). Another important observation is that the GLU behaves as an oxidizing agent in these three interactions and the Leu: GLU interaction is the most likely.

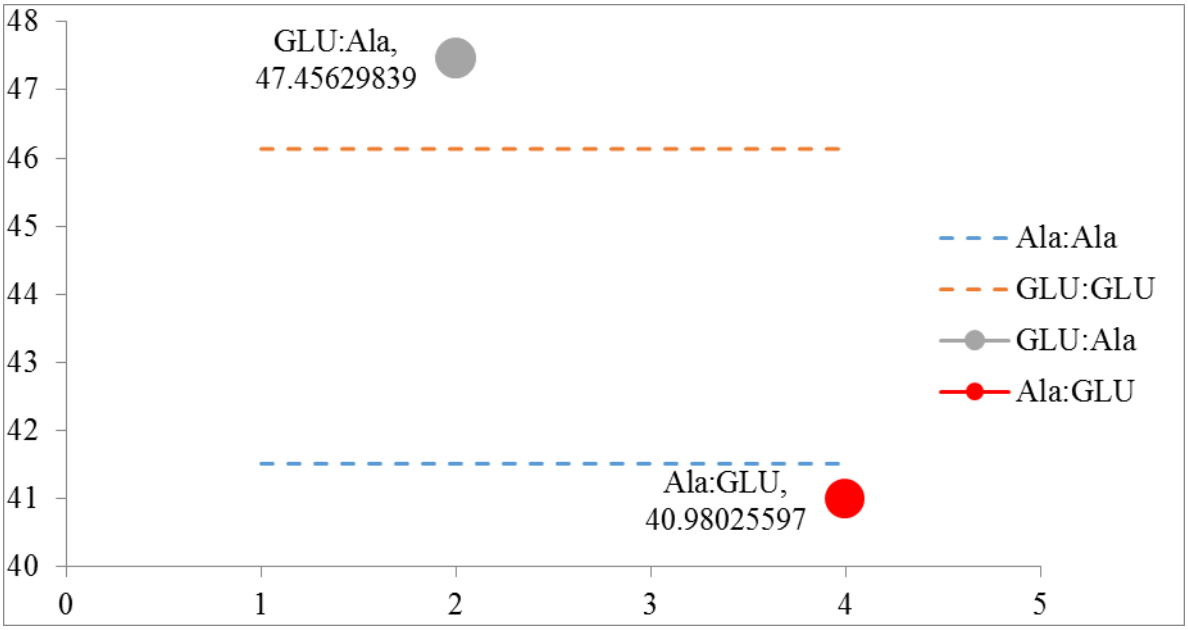

Figure 1: The Ala:GLU interaction is highly likely to take place too. This interaction occurs when GLU and Ala are found alone. GLU is an oxidizing agent in this interaction because its ETC is the lesser of both.

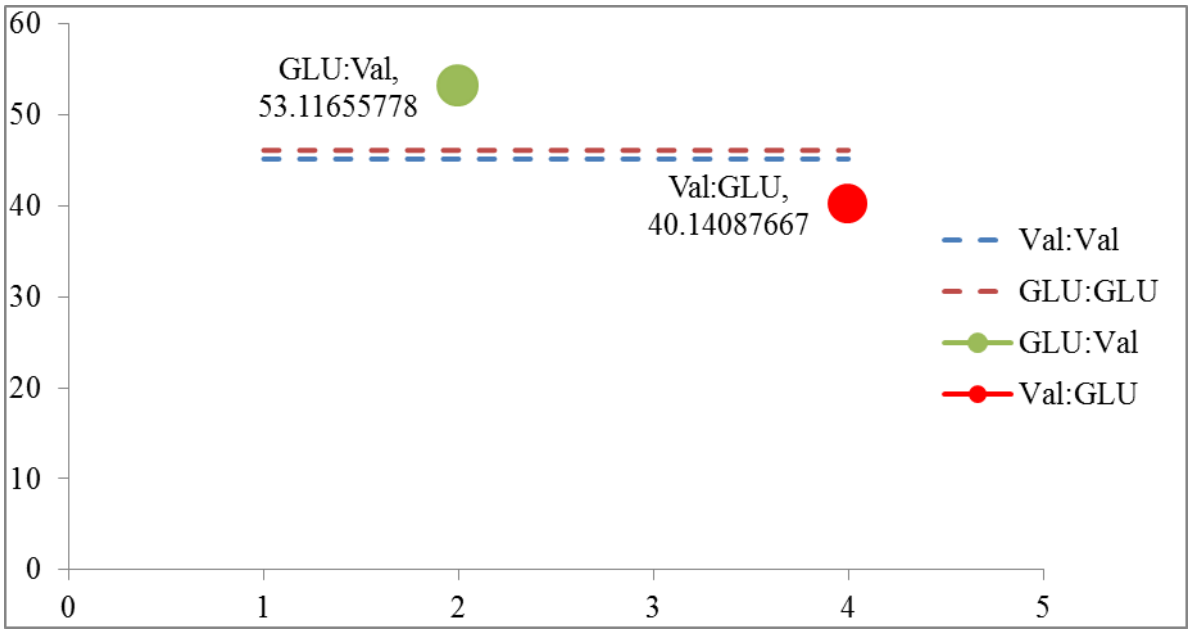

Figure 2: The Val:GLU interaction is highly likely to take place. This interaction occurs when GLU and Val are found alone. GLU is an oxidizing agent in this interaction because its ETC is the lesser of both.

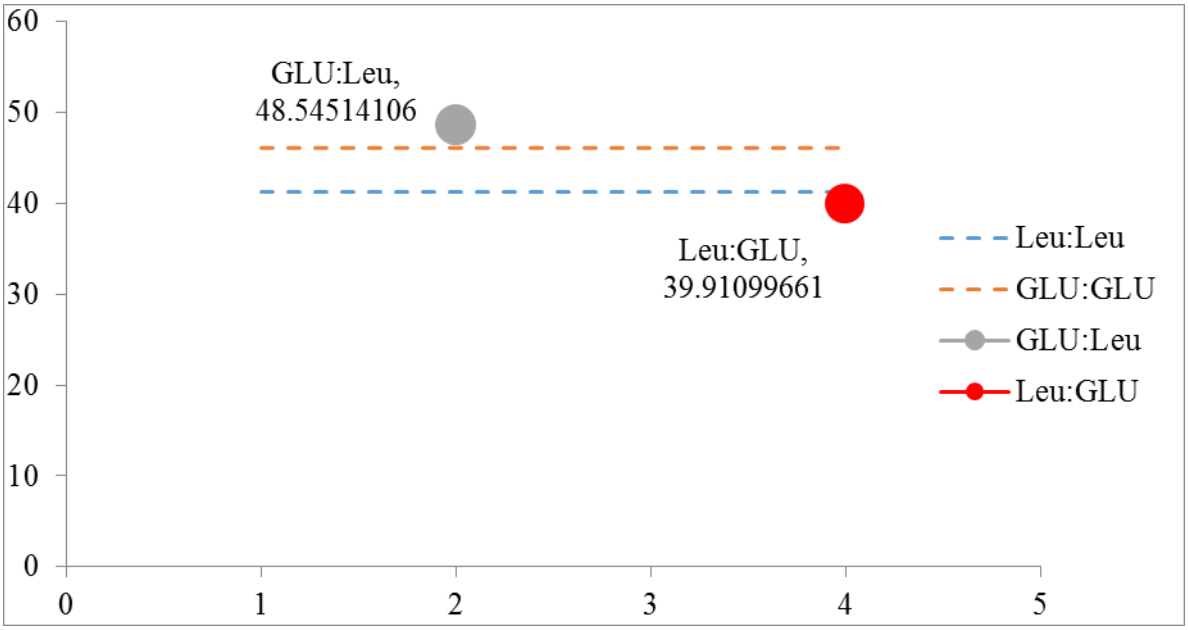

Figure 3: The Leu:GLU interaction is highly likely to take place too. This interaction occurs when GLU and Leu are found alone. GLU is an oxidizing agent in this interaction because its ETC is the lesser of both.

Figures 4, 5 and 6 show the lowest amino acid interactions of the 40 that were calculated. It is observed that all of them fall in a zone of average probability; however, the values of the ETCs of these interactions are lower than the one-to-one interactions (Fig. 1, 2, 3) of high probability.

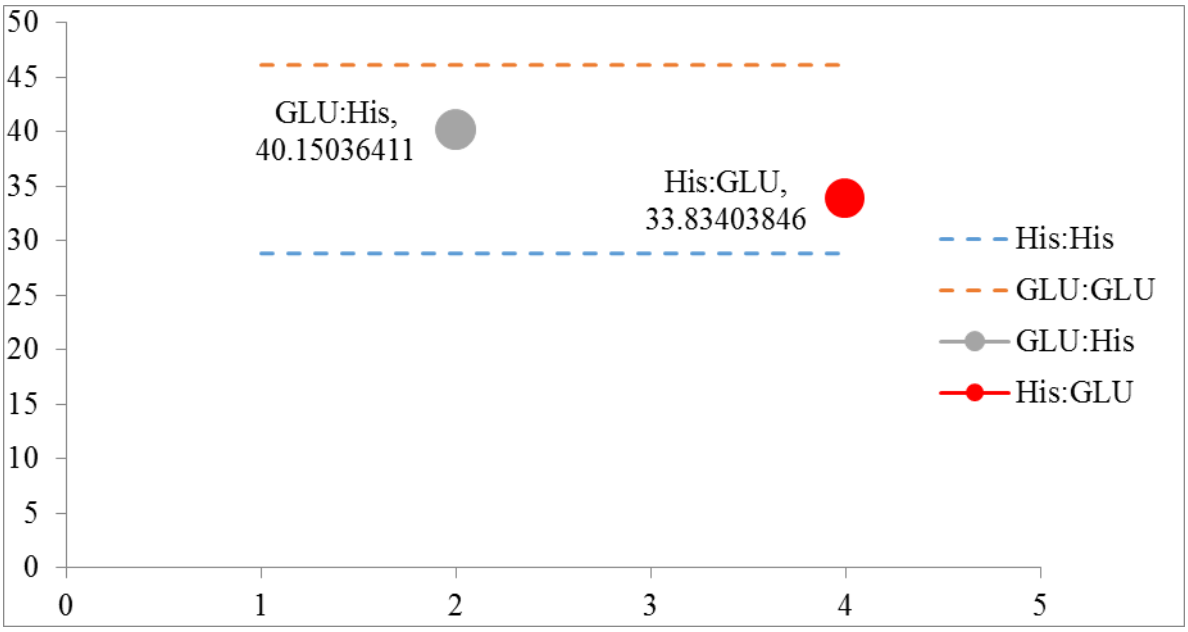

Figure 4: The interaction His:Glu occurs in the area of median probability; however, its ETC is lower than previous interactions.

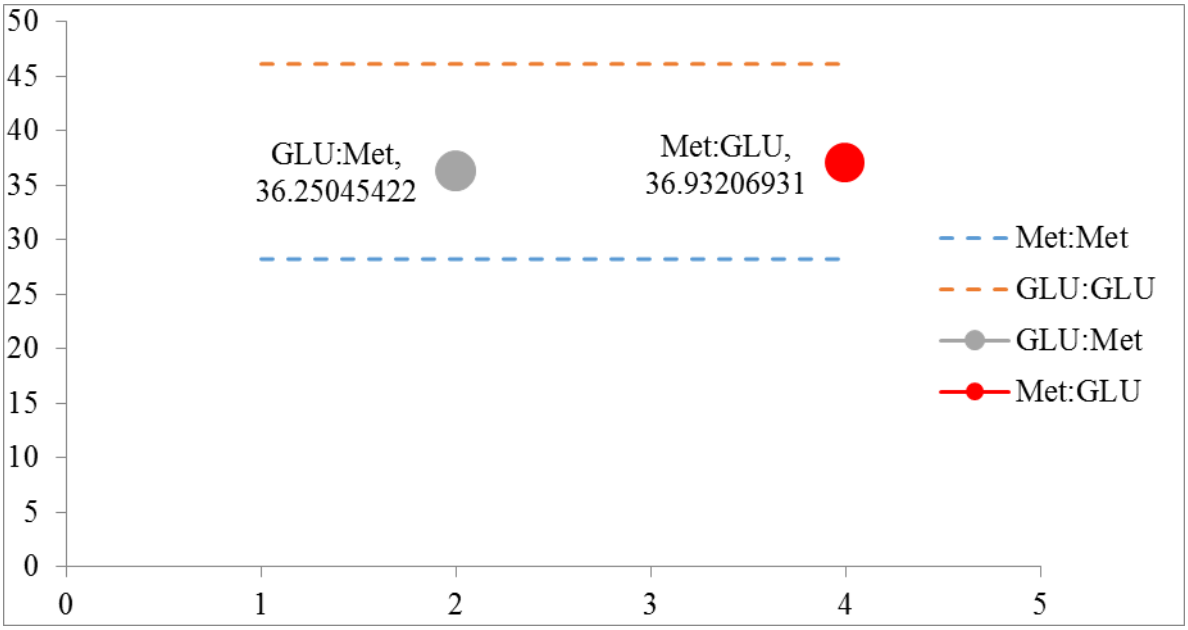

Figure 5: The interaction GLU:Met occurs in the area of median probability; however, its ETC is lower than previous interactions.

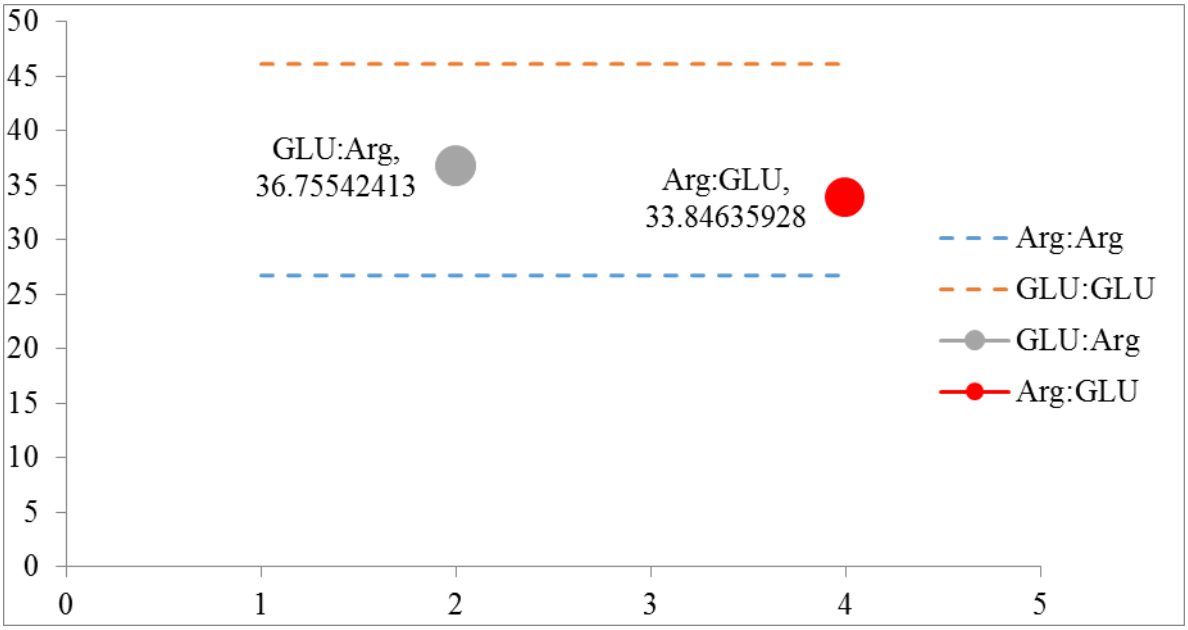

Figure 6: The interaction Arg:GLU occurs in the area of median probability; however, its ETC is lower than previous interactions.

Table 2: Summary of the GLU interactions of these six AAs.

Interaction X:GLU	The probability of irreversibility (due to the area of the quantum well)	Affinity probability (due to the value of your ETC)
X = Leu, Val, Ala	Very high	Low
X = His, Arg, Met	Half	High

Due to this apparent contradiction, 400 ETC calculations were made of pairs in a crossed band in order to observe the behavior of these AAs in enzymes such as insulin. These 400 ETCs were again crossed with HOMO of GLU, and LUMO of GLU, which resulted in another 800 ETC (AA1: AA2): GLU. Of these 800 ETCs, only three were observed. Table 3 summarizes the His block.

Table 3: ETCs of the interactions of the dipeptides compared with the dipeptides of His vs glucose.

No.	Reducing Agent	X = Oxidizing Agent	HOMO	LUMO	BG	E-	E+	EP	ETC
1	His	Val	-9.307	0.931	10.239	-0.169	0.109	0.278	36.830
2	His	Leu	-9.307	0.922	10.230	-0.169	0.130	0.299	34.212
3	***His - - X***	***GLU***	***-9.307***	***2.128***	***11.436***	***-0.169***	***0.169***	***0.338***	***33.834***
4	His**	Ala**	-9.307	0.749	10.057	-0.169	0.132	0.301	33.411
5	His	Phe	-9.307	0.283	9.591	-0.169	0.127	0.296	32.401
6	His	Gly	-9.307	0.902	10.209	-0.169	0.159	0.328	31.125
7	His	Cys	-9.307	-0.236	9.072	-0.169	0.140	0.309	29.359
8	His	Trp	-9.307	0.133	9.440	-0.169	0.155	0.324	29.136
9	His	His	-9.307	0.503	9.811	-0.169	0.171	0.340	28.855
10	His	Ile	-9.307	0.972	10.279	-0.169	0.188	0.357	28.793
11	His	Thr	-9.307	0.832	10.139	-0.169	0.191	0.360	28.165
12	His	Lys	-9.307	0.943	10.250	-0.169	0.195	0.364	28.160
13	His	Pro	-9.307	0.792	10.099	-0.169	0.191	0.360	28.054
14	His	Gln	-9.307	0.755	10.062	-0.169	0.192	0.361	27.873
15	His	Asn	-9.307	0.644	9.952	-0.169	0.193	0.362	27.491
16	His	Ser	-9.307	0.565	9.872	-0.169	0.198	0.367	26.900
17	His	Arg	-9.307	0.558	9.865	-0.169	0.199	0.368	26.808
18	His	Tyr	-9.307	0.293	9.600	-0.169	0.193	0.362	26.519
19	His	Glu	-9.307	0.438	9.746	-0.169	0.201	0.370	26.340
20	His	Met	-9.307	0.145	9.453	-0.169	0.192	0.361	26.184
21	His	Asp	-9.307	0.420	9.728	-0.169	0.204	0.373	26.079

The interaction (His: X): GLU keeps its ETC constant = 33.834 even if it changes the X to any of the AA.
*** This dipeptide is sold to the public under the name of L-Carnosine.*

In table 3. The interaction of cross-band AA pairs and the GLU can be observed. The pair (His: X) maintains a constant value of ETC = 33.834 although any of the 20 AA takes the

place of the X. This fact results in the stability of the pair of AA when it is subject in a higher entity such as insulin.

Interpretation of this phenomenon: The case of the block of Histidine (His:X): GLU is in the number 3 place ordered from highest to lowest. The pairs that are above 1 and 2: (His:Val) and (His:Leu) interact better with the GLU, hold it with more force; while the pairs that are below (from 4 to 20) release GLU more easily. ** L-Carnosine is a dipeptide (His:Ala) (number 4 in table 2) that is already on the market. This dipeptide is below the ETC = 33.824 constant value of the triad (His:X): GLU. The difference is 0.423 with the block constant (His:X): GLU. This difference leads us to think that the interaction is reversible by almost 50%; that is, subject or released to GLU almost as quickly.

A fundamental hypothesis derived from this research is that L-Carnosine has a function very similar to one of the active sites of insulin. However, it is not the only one.

CONCLUSIONS

All chemical-quantum calculations of the interactions between pure AAs were made and compared with the GLU.

Interactions of 400 dipeptides were also calculated, and they interacted in the cross-band with the GLU.

The following discoveries were made:

1. The GLU is very aggressive and can attack any AA in its pure state.
2. GLU also attacks dipeptides, polypeptides, and biological tissue.
3. Carnosine has an ETC = 33.824; there are other dipeptides with lower ETC.
4. All His dipeptides keep their ETC value = 33.824 constant, which is the ETC value of carnosine.

By studies of state of the art, the following hypothesis is stated to verify experimentally.
“All dipeptides of His must have similar behavior to carnosine.”

“Dipeptides of His have a very high probability of being the active site of insulin for glucose.” This is based on the fact that dipeptides of His have the lowest ETC of all dipeptides.

On the other hand, laboratory studies of these His dipeptides are suggested in order to control blood GLU and nephropathies for diabetic patients.

Note. If any person wishes to analyze the quantum chemical calculations extensively in intensive, please ask them to the corresponding author*:* manuel.gonzalez@upaep.mx.

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