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CHEMICAL-QUANTUM ANALYSIS OF BETA-CAROTENE AS ANTIOXIDANT FOR THE PREVENTION OF CANCER

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ABSTRACT

Cancer is a cellular disease of multicellular organisms. It is due to the alteration of the regulatory mechanisms in the cellular division of a tissue or an organ, thus producing damage in the cellular DNA, which exceeds the immune system function. This investigation aimed to make a chemical-quantum analysis of beta-carotene (Bcarot) as an antioxidant to prevent cancer. We used the semiempirical method Parametric Method 3 (SE-PM3) in hyperchem software as the basis for all calculations. This method treats the molecule as a collection of valence electrons and atomic centers; each center consists of an atom and its inner electrons. Bcarot ranks 18th among Amino Acids' stabilities (AAs) in biological proteins and forms a protective layer for AAs against free radicals. On the other hand, Bcarot forms a coat that can block the over-expression of Glucose 6 phosphate (G6P) in cancer cells. The layer that covers G6F is likely to inhibit the growth of a cancerous tumor. We concluded that adequate consumption of foods high in Bcarot helps patients with their cancerous conditions, and in people who do not have the disease, high consumption of Bcarot helps prevent it.

KEYWORD: Cancer, Beta-carotene, Quantum chemistry, PM3, Glucose 6 phosphate.

INTRODUCTION

Cancer is a cellular disease of multicellular organisms. It is due to the alteration of the regulatory mechanisms in the cellular division of a tissue or an organ, thus producing damage in the cellular DNA, which exceeds the immune system function.[1] The final product of

uncontrolled cell proliferation results from the accumulation of sequential genetic alterations (mutations) in a precursor cell. This cell population continues to mutate and perpetuate itself by secreting its growth factors and angiogenesis.[2]

Cancer encompasses different types of diseases characterized by abnormal cells' production in the human body, capable of dividing and potentially reproducing in any part of the body. Abnormal cells have a high capacity to invade organs and tissues and spread through the circulatory and lymphatic systems.[3]

According to different studies carried out in the clinical area in the last decades, the early detection of cancer has been achieved, saving thousands of lives; in the same way, technological development has paved the way for chemotherapy treatment antineoplastic drug administration.

Recent research studies suggest that chemoprevention is an alternative for patients who may have a genetic predisposition to develop cancer.

Cancer chemoprevention refers to the prevention or delay of the onset of carcinogenesis. The intervention of these agents helps to prevent, eliminate, or reverse malignant transformations. These substances must have an antioxidant effect; that is, they must partially slow down free radicals' activity.[4] The human organism has a series of endogenous antioxidant mechanisms; they are defensive mechanisms that control free radicals' action.

The vitamins A, C, E, Bcarot, and selenium are antioxidants. Plasma levels of antioxidants in food have been shown to have an inverse correlation with cancer mortality rates. Among the antioxidants found in certain foods, it is worth mentioning the following: Beta-carotene (provitamin A). It is fat-soluble, which is converted in the body into vitamin A, a powerful antioxidant. SOURCES: green vegetables (spinach, chard) and yellow (carrot, zucchini), cruciferous, garlic, parsley, livers.

It has been shown that this vitamin has preventive effects on cancer development.

Vitamin A comes from animal sources such as eggs, meat, milk, cheese, cream, liver, kidney, cod liver oil, and its hypoglossal nerve. However, all these food sources, except skim milk fortified with vitamin A, are high in saturated fats and cholesterol.

Sources of beta-carotene can be found in carrots, winter squash, sweet potatoes, sweet melon, zucchini, grapefruit, apricots, broccoli, spinach, and most green leafy vegetables. The more intense the color of the fruit or vegetable, the higher the carotenoid content.[5,6]

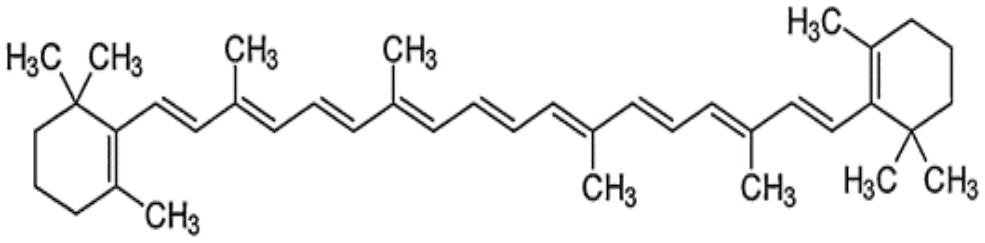
MATERIALS AND METHOD

HyperChem is a sophisticated molecular modeling environment known for its quality, flexibility, and ease of use. By combining 3D visualization and animation with quantum chemical calculations, molecular mechanics, and dynamics, HyperChem puts more molecular modeling tools at your fingertips than any other Windows program.[7]

SE-PM3 is used in hyperchem as the basis for all calculations. This method treats the molecule as a collection of valence electrons and atomic centers; each center consists of an atom and its inner electrons. The SE-PM3 method takes molecular valence energy, including internuclear repulsion, as the sum of purely electric energy.[8-16]

In figure 1, we present the schematics of the Bcarot molecule. In the electrostatic map (figure C), we can see that the positive poles predominate on the surface; however, this molecule is very apolar. This apolarity is due to the carbon and hydrogen bonds.

Figures 1D and 1E show HOMO and LUMO orbitals, respectively. These orbitals coincide in the same place. From this coincidence, it can be said that Bcarot forms spheres when it is a pure substance. Nevertheless, when it attacks the AAs in proteins, it can surround them in a layer.



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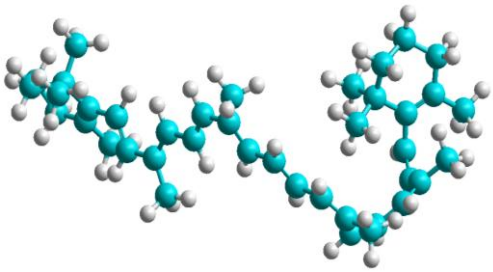

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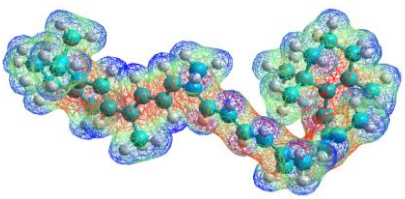

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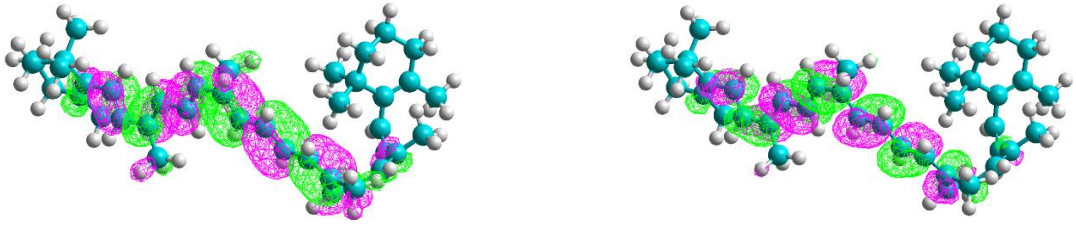

D E

Figure 1: Bcarot molecules in their different phases. A) Two-dimensional molecule. B) Simple three-dimensional molecule. C) Electrostatic potential. D) HOMO. E) LUMO.

RESULTS AND DISCUSSION

The first results are observed in table 1. This table represents a quantum well—their ETCs order AAs and Bcarot from highest to lowest. Interaction 1 is located at the bottom of the well; this interaction is of greater strength and probability. Therefore, Arg is the AA with the highest chemical stability, while Val is the AA with the lowest chemical stability.

The Bcarot is observed in the 18th place of the interactions. By this observation, it is said that this substance is not very stable concerning the other AAs.

Table 1: AAs and Bcarot ECTs ordered from lowest to highest.

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	Bcarot	Bcarot	-7.818	-0.948	6.870	-0.016	0.156	0.172	39.943
17	Phe	Phe	-9.553	0.283	9.836	-0.126	0.127	0.253	38.879
16	Gly	Gly	-9.902	0.902	10.804	-0.137	0.159	0.296	36.500
15	Ser	Ser	-10.156	0.565	10.721	-0.108	0.198	0.306	35.037
14	Cys	Cys	-9.639	-0.236	9.403	-0.129	0.140	0.269	34.956
13	Glu	Glu	-10.374	0.438	10.812	-0.111	0.201	0.312	34.655
12	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
10	Gln	Gln	-10.023	0.755	10.778	-0.124	0.192	0.316	34.108
9	Asp	Asp	-10.370	0.420	10.790	-0.118	0.204	0.322	33.509
8	Asn	Asn	-9.929	0.644	10.573	-0.125	0.193	0.318	33.249
7	Lys	Lys	-9.521	0.943	10.463	-0.127	0.195	0.322	32.495
6	Pro	Pro	-9.447	0.792	10.238	-0.128	0.191	0.319	32.095
5	Trp	Trp	-8.299	0.133	8.431	-0.112	0.155	0.267	31.577
4	Tyr	Tyr	-9.056	0.293	9.349	-0.123	0.193	0.316	29.584
3	His	His	-9.307	0.503	9.811	-0.169	0.171	0.340	28.855
2	Met	Met	-9.062	0.145	9.207	-0.134	0.192	0.326	28.243
1	Arg	Arg	-9.176	0.558	9.734	-0.165	0.199	0.364	26.742

Table 2 shows interactions 1-23 out of a total of 61 oxidation-reductive interactions. Bcarot appears as an oxidizing agent for all AAs in living beings. These interactions mean two things:

1. Bcarot protects AAs from attack by free radicals.
2. Bcarot blocks the enzyme kinase overexpressed in cancer cells.

The probable mechanism of this protection takes place due to the formation of a film. This film is formed by the most robust and most probable interaction shown in Table 2 (bottom of the quantum well).

Table 2: ETCs of amino acids and Bcarot ordered from smallest to largest.

N	Reducing agent	Oxidizing agent	Homo	Lumo	BG	E-	E+	EP	ETC
24…61									
23	Gln	Bcarot	-10.023	-0.948	9.075	-0.124	0.156	0.280	32.411
22	Pro	Pro	-9.447	0.792	10.238	-0.128	0.191	0.319	32.095
21	Thr	Bcarot	-9.896	-0.948	8.948	-0.123	0.156	0.279	32.073
20	Asn	Bcarot	-9.929	-0.948	8.981	-0.125	0.156	0.281	31.961
19	Ala	Bcarot	-9.879	-0.948	8.931	-0.124	0.156	0.280	31.896
18	Trp	Trp	-8.299	0.133	8.431	-0.112	0.155	0.267	31.577
17	Ile	Bcarot	-9.872	-0.948	8.924	-0.128	0.156	0.284	31.423
16	Val	Bcarot	-9.914	-0.948	8.966	-0.131	0.156	0.287	31.240
15	Leu	Bcarot	-9.645	-0.948	8.697	-0.126	0.156	0.282	30.842
14	Gly	Bcarot	-9.902	-0.948	8.954	-0.137	0.156	0.293	30.561
13	Phe	Bcarot	-9.553	-0.948	8.605	-0.126	0.156	0.282	30.514
12	Cys	Bcarot	-9.639	-0.948	8.691	-0.129	0.156	0.285	30.494
11	Lys	Bcarot	-9.521	-0.948	8.573	-0.127	0.156	0.283	30.292
10	Pro	Bcarot	-9.447	-0.948	8.499	-0.128	0.156	0.284	29.924
9	Tyr	Tyr	-9.056	0.293	9.349	-0.123	0.193	0.316	29.584
8	Tyr	Bcarot	-9.056	-0.948	8.108	-0.123	0.156	0.279	29.061
7	His	His	-9.307	0.503	9.811	-0.169	0.171	0.340	28.855
6	Met	Met	-9.062	0.145	9.207	-0.134	0.192	0.326	28.243
5	Met	Bcarot	-9.062	-0.948	8.114	-0.134	0.156	0.290	27.979
4	Trp	Bcarot	-8.299	-0.948	7.351	-0.112	0.156	0.268	27.427
3	Arg	Arg	-9.176	0.558	9.734	-0.165	0.199	0.364	26.742
2	His	Bcarot	-9.307	-0.948	8.359	-0.169	0.156	0.325	25.721
1	Arg	Bcarot	-9.176	-0.948	8.228	-0.165	0.156	0.321	25.633

Table 3 shows the characterization of insulin and G6F.[17] The interactions of 4 of the AAs most representative of each of them are compared. In all, the Bcarot gains the interaction by the AAs of both insulin and kinase. Therefore, Bcarot displaces both GLU and a molecule of the same AA species.

Table 3: Comparison of the interactions of four ALAs in competition for their substance, by GLU and Bcarot.

N	AA	Insulin	G6P	ETCs Pure	ETCs GLU	ETCs Bcarot	Reaction	Observaciones
1	Ala	10	40	41.515				
2	**Arg*	*5*	*27*	*26.742*	*33.845*	*25.633*	*Oxidation*	*Arg prefers Bcarot*
3	Asn	3	28	33.249				
4	Asp	2	27	33.509				
5	Cys	6	4	34.956				
6	Gln	7	29	34.108				
7	Glu	8	32	34.655				
8	Gly	12	41	36.500				
9	**His*	*2*	*21*	*28.855*	*33.833*	*25.721*	*Oxidation*	*His prefers Bcarot*
10	Ile	2	32	34.316				
11	**Leu*	*20*	*54*	*41.279*	*39.909*	*30.842*	*Oxidation*	*Leu prefers Bcarot*
12	Lys	2	35	32.495				
13	Met	2	14	28.243				
14	Phe	3	27	38.879				
15	Pro	6	22	32.095				
16	Ser	5	29	35.037				
17	Thr	3	37	34.167				
18	Trp	2	14	31.577				
19	Tyr	4	14	29.584				
20	*Val	*6*	*32*	*45.188*	*40.139*	*31.240*	*Oxidation*	*Val prefers Bcarot*

** Most representative interactions of insulin and G6F proteins. Note that Bcarot competes for GLU and wins the interaction due to its low ETC.*

Table 4 shows that Bcarot does not appear among the first 21 interactions of the 55 in a total of the quantum well. These interactions only occur between the nitrogenous bases of DNA and RNA. With this observation, it can be said that Bcarot is not mutagenic.

Tabla 4: Fondo del pozo cuántico de las atracciones de las bases nitrogenadas y el Bcarot.

N	Reducing agent	Oxidizing agent	HOMO	LUMO	BG	E-	E+	EP	ETC
21	A	C	-8.654	-0.344	8.310	-0.140	0.161	0.301	27.610
20	U2	U2	-9.910	-0.415	9.495	-0.147	0.202	0.349	27.208
19	U2	U2	-9.910	-0.415	9.495	-0.147	0.202	0.349	27.206
18	G	A	-8.537	-0.213	8.324	-0.150	0.156	0.306	27.202
17	A	G	-8.654	-0.206	8.448	-0.140	0.172	0.312	27.078
16	C	A	-9.142	-0.213	8.929	-0.174	0.156	0.330	27.058
15	A	T	-8.654	-0.475	8.179	-0.140	0.169	0.309	26.471
14	G	C	-8.537	-0.344	8.193	-0.150	0.161	0.311	26.345
13	C	C	-9.142	-0.344	8.798	-0.174	0.161	0.335	26.265
12	C	C	-9.142	-0.344	8.798	-0.174	0.161	0.335	26.263

11	A	U1	-8.654	-0.511	8.143	-0.140	0.171	0.311	26.185
10	G	G	-8.537	-0.206	8.331	-0.150	0.172	0.322	25.873
9	G	G	-8.537	-0.206	8.331	-0.150	0.172	0.322	25.872
8	C	G	-9.142	-0.206	8.936	-0.174	0.172	0.346	25.827
7	G	T	-8.537	-0.475	8.062	-0.150	0.169	0.319	25.273
6	C	T	-9.142	-0.475	8.667	-0.174	0.169	0.343	25.270
5	C	U1	-9.142	-0.511	8.631	-0.174	0.171	0.345	25.019
4	G	U1	-8.537	-0.511	8.026	-0.150	0.171	0.321	25.003
3	A	U2	-8.654	-0.415	8.239	-0.140	0.202	0.342	24.092
2	C	U2	-9.142	-0.415	8.727	-0.174	0.202	0.376	23.212
1	G	U2	-8.537	-0.415	8.122	-0.150	0.202	0.352	23.074

CONCLUSIONS

We did

1. Calculations of ETCs for Bcarot and AAs for insulin and G6F enzyme (Table 1).
2. ETCs calculations for oxidation-reduction interactions of AAs and G6F (Table 2).
3. The calculations of the ETCs of the interactions of the Bcart and the nitrogenous bases. (Table 4).
4. We compared the ETCs for the competition of GLU and Bcart for the AAs of insulin and G6F (Table 3).

We find that

1. Bcarot ranks 18th among the stabilities of AAs in biological proteins.
2. Bcarot forms a protective layer for AAs against free radicals.
3. Bcarot forms a coat that can block the over-expression of G6F in cancer cells.
4. The layer that covers G6F is likely to inhibit the growth of a cancerous tumor.

We concluded that adequate consumption of foods high in Bcarot helps patients with their cancerous conditions, and in people who do not have the disease, high consumption of Bcarot helps prevent it.

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