WORLD JOURNAL OF PHARMACEUTICAL RESEARCH
SJIF Impact Factor 8.084
Volume 12, Issue 12, 14-23. Research Article ISSN 2277– 7105

CHEMICAL-QUANTUM CHARACTERIZATION OF CYCLOPHOSPHAMIDE VS. AMINO ACIDS OF THE HUMAN BODY

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Article Received on
25 May 2023,

Revised on 15 June 2023,
Accepted on 05 July 2023

DOI: 10.20959/wjpr202312-28935

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ABSTRACT

Cyclophosphamide (CPM) is a chemotherapeutic agent first discovered in experimental tumors in rats and has since been widely used to treat malignancies and severe manifestations of various autoimmune diseases. The aim was to characterize CPM Amino acids (AA) from the human body by quantum chemistry, to assess whether CPM is an anticancer agent. Hyperchem software was used as a quantum chemistry simulator. The fundamental basis of quantum calculations was the theory of the electron transfer coefficient (ETC). We can see the ETCs ordered according to the quantum well. It is observed that the CPM is located at the bottom of the well. This location leads us to infer that CPM is a long-acting substance; in other words, it is difficult to remove from the biological system. The information in the whisker and box plots shows that the probability of oxidative interactions occurring is very high because they are located at the bottom of the quantum well. We found that CPM is a potent oxidant of AAs in the human body; for this reason, it is used as an anticancer chemotherapeutic agent.

KEYWORD: CPM, Chemical-quantum, Amino acid, Human body, Cancer.

INTRODUCTION

CPM is a chemotherapeutic agent first discovered in experimental tumors in rats and has since been widely used to treat malignancies and severe manifestations of various autoimmune diseases.[1,2] High-dose chemotherapy and continuous daily oral regimens are associated with significant toxicity profiles, but intravenous pulsed regimens have reduced adverse effect rates in rheumatology studies.[3,4] Due to its powerful immunosuppressive capacity, CPM is useful in treating severe autoimmune diseases.[5,6]

AAs are a group of organic molecules consisting of a basic amino group (—NH2), an acidic carboxyl group (—COOH), and an organic R group (or side chain) that is unique to each AA.[7] The term AA is short for α-amino [alpha-amino] carboxylic acid.[8] Each molecule contains a central carbon atom (C), called the α carbon, to which an amino and carboxyl group is attached.[9] The two remaining bonds of the α carbon atom are generally satisfied with a hydrogen atom (H) and the R group.[10,11]

The use of a mixture of AAs caused a selective induction of apoptosis against various tumor cell lines, reduced the adverse effects of anticancer drugs, and increased the sensitivity of tumor cells to chemotherapeutic agents.[12] We evaluated the effects and underlying mechanisms of oral supplementation of soy-derived multiple AAs on the therapeutic efficacy of low-dose CPM and tumor growth, apoptosis, and autophagy in severe combined immunodeficiency (SCID) mice. That were injected with sarcoma-180 (S-180) cells.[13] 3-methyladenine or siRNA knockdown of Atg5 was used to assess its effect on sarcoma growth. A comparison of mice with implanted sarcoma cells, CPM, and oral saline and mice with implanted sarcoma cells, CPM, and an oral soy-derived multi-AA supplement indicated that the soy-derived multi-AA supplement significantly decreased the overall sarcoma growth, increased Bax/Bcl-2 ratio, caspase three expression and apoptosis, and depressed LC3 II-mediated autophagy.[14] Treatment with 3-methyladenine or Atg5 siRNA elicited similar responses to CPM plus soybean-derived multiple AAs in downregulating autophagy and upregulating apoptosis. A low dose of CPM combined with an oral supplement of soybean-derived multiple AAs had a potent antitumor effect mediated by the downregulation of autophagy and upregulation of apoptosis.[15]

MATERIAL AND METHODS

Hyperchem software was used as a quantum chemistry simulator. The fundamental basis of quantum calculations was the theory of the ETC. For the specific calculations of HOMO and

LUMO, the semi-empirical parametric method 3 was used. The Polak Ribiere simulator was used to minimize energy.

For the calculation of the electrostatic potential, the Plot Molecular Graph method in three dimensions was used.

Finally, the ETC was calculated by dividing the band gap by the electrostatic potential.

As there are too many calculations, only the tables and the whisker and box diagrams are presented in this article. If you would like more information, please contact Dr. González.

Interpretation of the quantum well

Figure 1 presents the quantum well of the interactions through its ETC. On the left side the antioxidant or reducing interactions are shown, on the right side the oxidant interactions. This well is divided into four quadrants, ordered from lowest to highest from bottom to top. The deeper interactions in the well are of greater chemical affinity and probability of occurring.

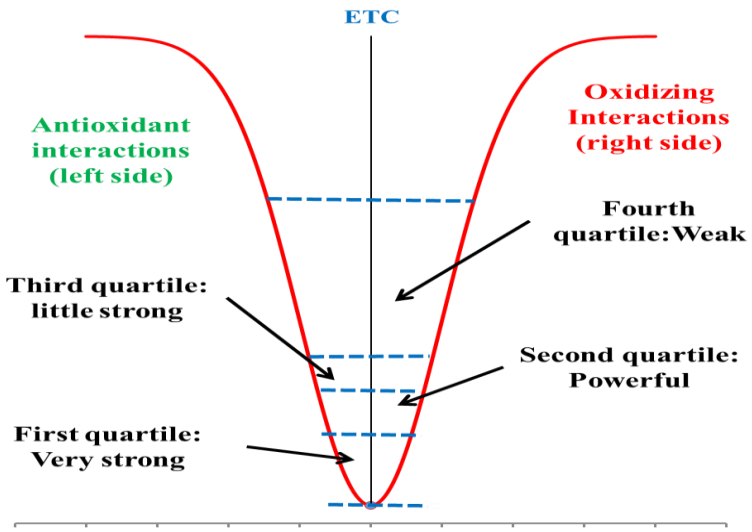
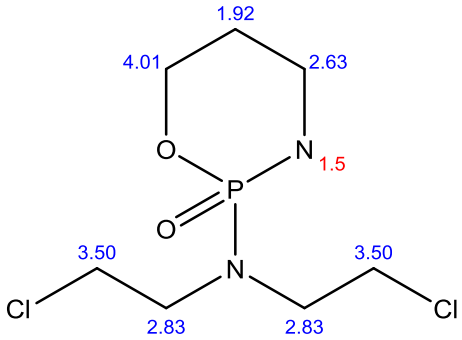


Figure 1: Quantum well. Interpretation of the interactions in the four statistical quadrants.

RESULTS AND DISCUSSION

Classic characterization

Figure 2 shows the results of the simulated characterization of H Nuclear Magnetic Resonance and the scientific name according to the UIPAC of CPM.



2-(bis(2-chloroethyl)amino)-1,3λ^2,2-oxazaphosphinane 2-oxide

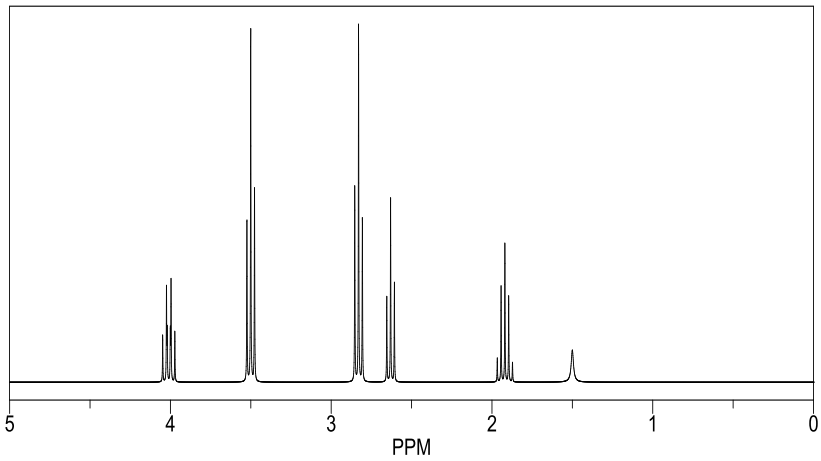
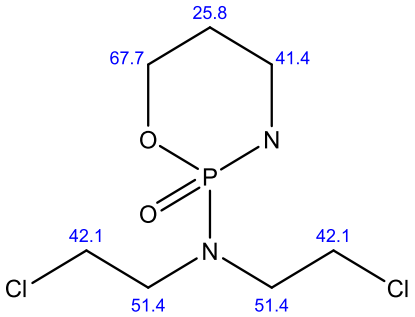


Figure 2: Scientific name UIPAC and Nuclear Magnetic Resonance of H. Above the molecule with its quantified protons. Below is the multiplicity diagram of protons.

Figure 3 shows the results of the simulated characterization of C13 Nuclear Magnetic Resonance.



2-(bis(2-chloroethyl)amino)-1,3λ^2,2-oxazaphosphinane 2-oxide

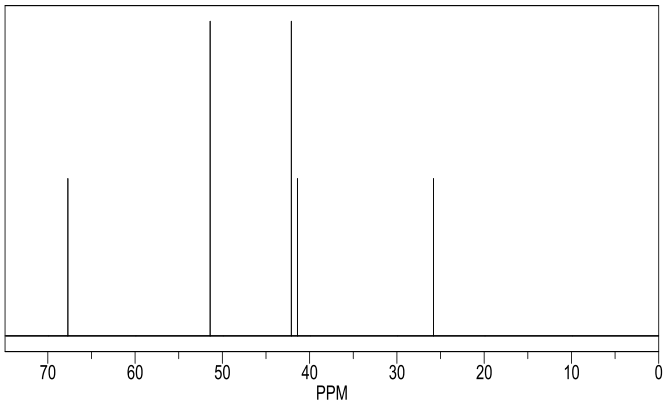
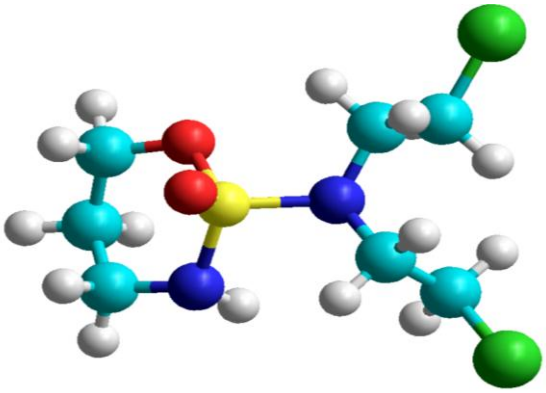


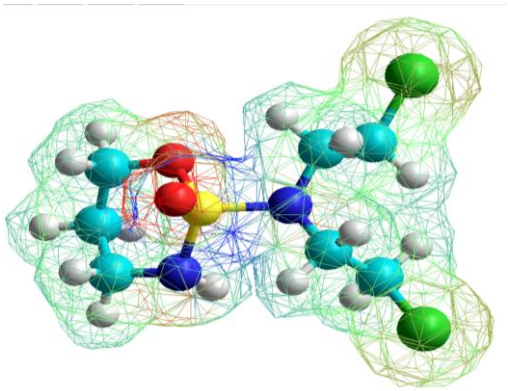
Figure 3: C13 nuclear magnetic resonance. At the top the molecule is shown with its quantified Carbons and At the bottom is the diagram in ppm.

Quantum characterization

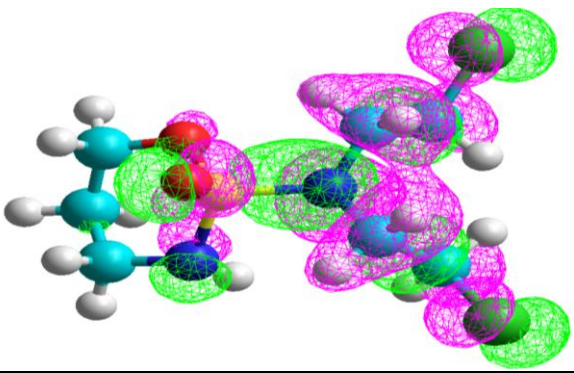
Figure 4 shows us the CPM molecule characterized in its different quantum concepts. This molecule presents quantum superposition of HOMO and LUMO. This quantum property infers that it has spheres or micelles.



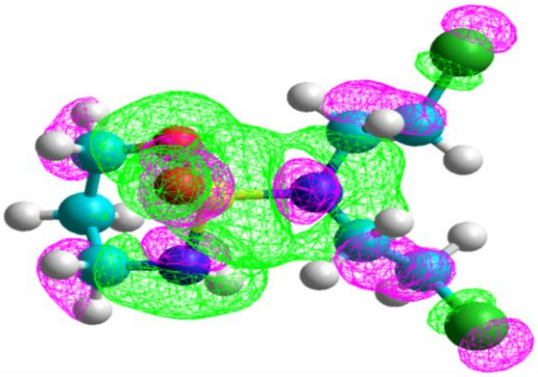
a. Cyclophosphamide. Hyperchem.



b.Cyclophosphamide. electrostatic potential. -δ = 0.170 eV/a°; +δ = 0.291 eV/a°



c. Cyclophosphamide. HOMO. -9.877 eV



d. Cyclophosphamide. LUMO. -0.373 eV

Figure 4. Quantum characterization. A) Cyan = C; White = Y; Red = O; Yellow = P, Blue = N; Green = Cl.

Quantum calculations

BG = |HOMO-LUMO| Eq. 1.

EP = |(–δ) – (+δ)| Eq. 2.

ETC = BG/EP Eq. 3.

Where:

BG = band gap. Column 6 of table 1.

EP = electrostatic potential. Column 9 of table 1.

ETC = Electron Transfer Coefficient. Column 10 of table 1.

Each line of table 1 was made with these calculations. The whisker and box plot are the summary of 61 interactions between CPM and the 20 AAs of the human body.

In table 1, we can see the ETCs ordered according to the quantum well. It is observed that the CPM is located at the bottom of the well. This location leads us to infer that CPM is a long-acting substance, in other words, it is very difficult to remove from the biological system.[16-20]

Table 1: ETCs of pure substances AAs and CPM.

N	Reducing agent	Oxidizing agent	HOMO	LUMO	BG	–δ	+δ	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	CPM	CPM	-9.877	-0.373	9.504	-0.170	0.291	0.461	20.617

Figure 5 provides us with the information in whisker and box plots. The upper left diagram shows the reducing or antioxidant interactions and the lower right diagram shows the oxidative interactions. The probability of oxidative interactions occurring is very high, because they are located at the bottom of the quantum well.

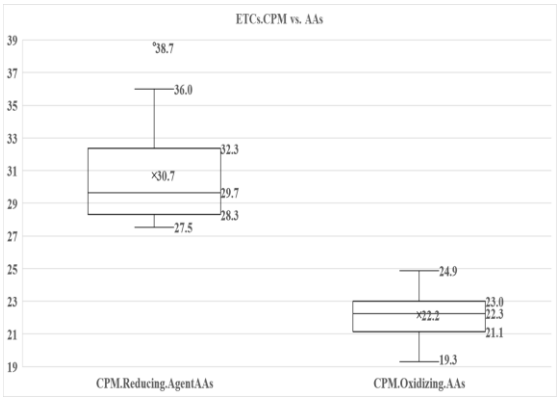


Figure 5: Whisker plots of the ETCs of quantum-chemical interactions. The lower right diagram indicates that the interactions are 100% oxidizing in nature.

CONCLUSIONS

Aim. To characterize CPM and AAs from the human body by quantum chemistry, to assess whether CPM is an anticancer agent.

Thesis. We found that CPM is a potent oxidant of AAs in the human body, for this reason it is used as an anticancer chemotherapeutic agent (figure 5).

Corollary. We found outside our objective that CPM is a long-acting drug and for that reason it is very difficult to eliminate from the body (Table 1).

ACKNOWLEDGMENTS

To our parents, who with their example of tenacity, honesty and love guide us along the path of life.

To the Delfín program for giving us the opportunity to scientifically investigate these substances that are so important for stopping cancer.

To the Technological University of Tecamachalco for providing us with its facilities, intellectual and logistical support in general, to develop this important research.

To the Universidad Autónoma de Chiapas, Universidad Veracruzana, TecNM campus Acapulco, our alma mater.

To our teachers, unconditional guides to the progress of us, our community, and our country Mexico.

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