EVALUATION OF THE INTERACTION OF THREE TYPES OF ANTRACICLINES AND NEUROTRASMISORS USING QUANTIC CHEMICAL SIMULATION

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RESUMEN

En este trabajo analizamos tres tipos de antraciclinas (ACys). El análisis consiste en observar cómo estos ACys interactúan con los neurotransmisores (NT). Estos medicamentos se usan en el tratamiento de diferentes tipos de cáncer en pacientes humanos. El programa Hyperchem se utilizó para realizar la simulación y los cálculos de variables cuánticas. Como resultado, los investigadores observamos que ACys tiene una alta probabilidad de interacción con NT. Esta interacción tiene diferentes efectos posibles dependiendo del compuesto que se analiza. Llegamos a la conclusión de que la parte del sistema nervioso central (SNC) que controla el estado de ánimo del paciente se ve afectada.

Palabra clave. Antraciclinas, neurotransmisores, Hyperchem, análisis cuántico

ABSTRACT

In this work we analyze three types of anthracyclines (ACys). The analysis consists of observing how these ACys interact with the neurotransmitters (NT). These drugs are used in the treatment of different types of cancer in human patients. The Hyperchem program was used to perform the simulation and calculations of quantum variables. As a result, we researchers observed that ACys have a high probability of interaction with NT. This interaction has different possible effects depending on the compound being analyzed. We conclude that the part of the central nervous system (CNS) that controls the mood of the patient is affected.

Keyword. Anthracyclines, Neurotransmitters, Hyperchem, Quantum Analysis

1. INTRODUCTION

Clinical use of the three ACys

Daunorubicin is a chemotherapeutic drug of the ACy family that is used to treat certain types of cancer. Some specific types of leukemia, such as acute myeloid leukemia and acute lymphoid leukemia [4].

Epirubicin is a medication that belongs to the ACy family and is used as chemotherapy to treat cancer. It causes fewer side effects due to its rapid elimination. It is primarily used in the treatment of breast cancer, ovarian cancer, stomach cancer, lung cancer and lymphomas [5-8].

Doxorubicin is a drug that belongs to the ACy family and is used as chemotherapy to treat cancer. Doxorubicin is commonly used in the treatment of some leukemia and Hodgkin's lymphoma, as well as cancer of the bladder, breast, stomach, lung, ovaries, thyroid, multiple myeloma and others [9-11].

Currently, there are no known studies that predict the effects of ACys on NT or AA. On the other hand, ACys attack DNA synthesis and replication, but very little is known about the active site of the attack to break the chain [12-13].

In the other hands, NTs are chemicals created by the body that transmit information signals from a neuron through contact points called synapses. The knowledge about neurotransmitters is fundamental to understand the human being. It is linked to the nervous system and the adaptation of the mind to each process [14-16].

Therefore, the article focuses on the quantum analysis of three basic types of ACys used for different types of cancer and the possible chemical interaction of compounds with the main neurotransmitters [17-20].

We perform an analysis of the ACys to know how they affect human body functions.
For this, the HYPERCHEM quantum interaction program is used, which is a quantum analysis tool to compare compounds in pairs using their chemical characteristics [21-24].

2. MATERIALS AND METHODS

This article was evaluated by researchers for three different types of ACys most commonly used as drugs against different types of cancer. The neurotransmitters that we choose for this analysis are the most representative.

It selected specific parameters for each of the simulations shows in Table 1 and 2 [26].

Table 1. Parameters used for quantum computing molecular orbitals HOMO and LUMO and BG

Parameter	Value	Parameter	Value
Total Charge	0	Polarizability	Not
Spin Multiplicity	1	Geometry Optimization: Algoritm	Polak-Ribiere (Conjugated gradient)
Spin Pairing	RHF	Termination condition RMS gradient of	0.1 kcal/Amol
State Lowest Converget Limit	0.01	Termination condition or	195 maximum cycles
Interation Limit	50	Termination condition or	In vacuo
Accelerate Convergence	Yes	Screen refresh period	1 cyclest

Table 2. Parameters used for quantum computing E-, E+ and EP

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 Layaout	Default	Isosurface Rendering: Total charge density contour value	0.015
Contour Grid: Starting Value	Default	Rendering Wire Mesh	Default

3. RESULTS AND DISCUSSION

Table 3 shows the interactions of all the pure substances selected for this study. It can be seen that DAUNORUBICIN is the most chemically stable drug; while ACETYLCHOLINE is the most unstable NT of all of them.

In ascending order, greater stability is noted in the EPIRUBICIN than in the DOXORUBICIN. However, ADRENALINE is interspersed among the three drugs. For this reason, it is assumed that ADRENALINE can be attacked by them very quickly.

Table 3. ETCs of pure substances. The DAUNORUBICIN is the most stable of all.
The ACETYLCHOLINE is the most unstable of all

SUBSTANCE	HOMO	LUMO	BG	E-	E+	EP	ETC
ACETYLCHOLINE	-9.242	1.034	10.276	-0.028	0.105	0.133	77.265
NORADRENALINE	-9.152	-0.004	9.148	-0.083	-0.222	0.139	65.810
GLUTAMIC ACID	-10.044	0.537	10.582	-0.084	0.197	0.281	37.657
ASPARTIC ACID	-10.242	0.516	10.758	-0.109	0.198	0.307	35.042
GLYCINE	-9.853	0.874	10.727	-0.126	0.188	0.314	34.164
GABA	-9.562	0.939	10.500	-0.140	0.180	0.320	32.813
DOPAMINE	-8.868	0.199	9.067	-0.098	0.189	0.287	31.591
SEROTONINE	-8.948	-0.129	8.819	-0.145	0.141	0.286	30.836
DOXORUBICIN*	-9.299	-0.605	8.694	-0.115	0.186	0.301	28.885
ADRENALIN	-8.998	0.092	9.090	-0.117	0.198	0.315	28.858

EPIRUBICIN*	-8.932	-1.235	7.696	-0.109	0.187	0.296	26.000
DAUNORUBICIN*	-8.955	-1.293	7.662	-0.137	0.188	0.325	23.575

*The drugs that interact with NTs.

In table 4 we can see the molecule-to-molecule interactions of drugs and NTs. It is important to note that the interactions of the three drugs show a similar pattern. It can be seen in this table that the medicines oxidize the NT with a very high probability. However, NTs have a very low likelihood of oxidizing all three drugs.

We designed, figures 1, 2, 3, and four were to clarify with more precision this event; They illustrate a similar pattern where each NT gives electrons to drugs. Serotonin is the most affected by drugs, then followed by GABA, ADRENALINE, DOPAMINE, GLYCINE.

On the other hand, some interactions between drugs are observed. These undesired interactions may cause a potential deficiency or an increase in the potential of the drugs for their therapeutic effect or their unwanted side reactions (interactions: 60, 54, 53, 49 table 4).

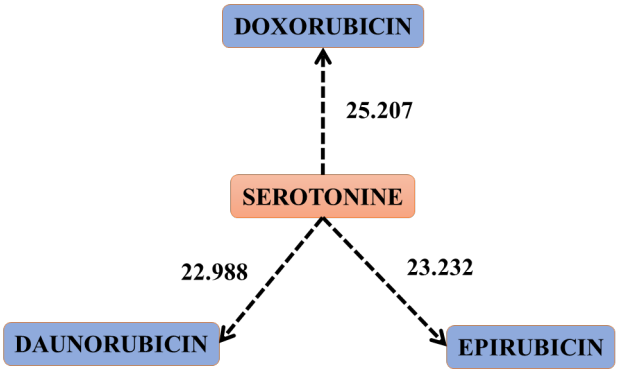

Figure 1. The scheme that shows the jump of electrons or electronic clouds from serotonin to the three drugs. Interactions: 59, 62 and 63 of table 4. This figure represents the oxidation of SEROTONINE by the three drugs

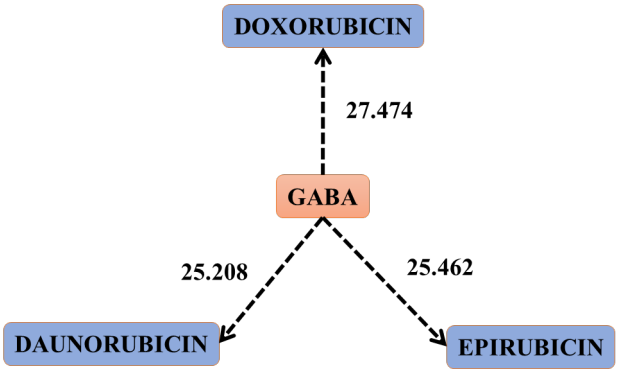

Figure 2. Scheme that shows the jump of electrons or electronic clouds from GABA to the three drugs. Interactions: 58, 56 and 45 of table 4. This figure represents the oxidation of GABA by the three drugs

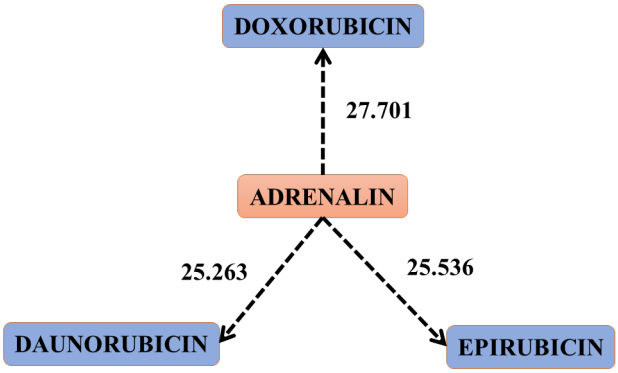

Figure 3. Scheme that shows the jump of electrons or electronic clouds from ADRENALIN to the three drugs. Interactions: 57, 55 and 43 of table 4. This figure represents the oxidation of ADRENALIN by the three drugs

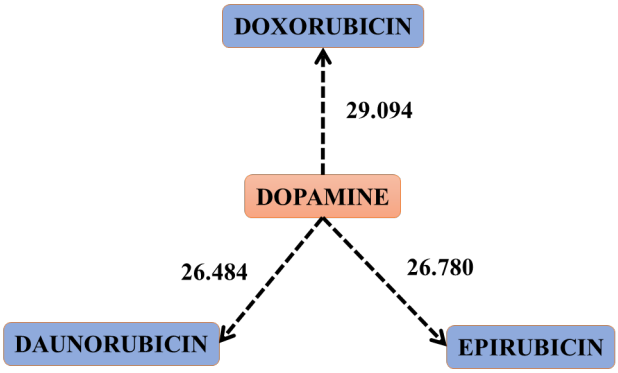

Figure 4. Scheme that shows the jump of electrons or electronic clouds from DOPAMINE to the three drugs. Interactions: 50, 48 and 36 of table 4. This figure represents the oxidation of DOPAMINE by the three drugs

SEROTONIN is known as a very important NT and is related to the state of mind that a person can adopt. There may be a depressive effect in patients who undergo treatment with the 3 drugs. Similarly, ADRENALIN is one of the best known NT and is responsible for increasing the metabolism and alerting it if there is any danger. When interacting with this tree, it could cause a deficit of energy in the patients that would lead to low levels of metabolism in the body. On the other hand, GABA affects the nervous system, which corroborates the above.

Table 4. The ETCs or crossed bands. It is observed that the NT most oxidized by th drug DAUNORUBICIN is the serotonin

	SUBSTANCE								
No	**REDUCING AGENT**	**OXIDIZING AGENT**	**HOMO**	**LUMO**	**BG**	**E-**	**E+**	**EP**	**ETC**
1	DAUNORUBICIN	NORADRENALINE	-8.955	-0.004	8.951	-0.137	-0.222	0.085	105.303
2	DOXORUBICIN	NORADRENALINE	-9.299	-0.004	9.295	-0.115	-0.222	0.107	86.870
3	EPIRUBICIN	NORADRENALINE	-8.932	-0.004	8.927	-0.109	-0.222	0.113	79.003
4	DOXORUBICIN	ACETYLCHOLINE	-9.299	1.034	10.334	-0.115	0.105	0.220	46.971
5	EPIRUBICIN	ACETYLCHOLINE	-8.932	1.034	9.966	-0.109	0.105	0.214	46.569
6	DAUNORUBICIN	ACETYLCHOLINE	-8.955	1.034	9.989	-0.137	0.105	0.242	41.278
7	ACETYLCHOLINE	DOXORUBICIN	-9.242	-0.605	8.637	-0.028	0.186	0.214	40.360
8	ACETYLCHOLINE	EPIRUBICIN	-9.242	-1.235	8.007	-0.028	0.187	0.215	37.240

9	ACETYLCHOLINE	DAUNORUBICIN	-9.242	-1.293	7.949	-0.028	0.188	0.216	36.800
10	DOXORUBICIN	SEROTONINE	-9.299	-0.129	9.170	-0.115	0.141	0.256	35.820
11	EPIRUBICIN	SEROTONINE	-8.932	-0.129	8.802	-0.109	0.141	0.250	35.209
12	GLUTAMIC ACID	DOXORUBICIN	-10.044	-0.605	9.439	-0.084	0.186	0.270	34.961
13	DOXORUBICIN	GABA	-9.299	0.939	10.238	-0.115	0.180	0.295	34.705
14	EPIRUBICIN	GABA	-8.932	0.939	9.870	-0.109	0.180	0.289	34.153
15	DOXORUBICIN	GLYCINE	-9.299	0.874	10.174	-0.115	0.188	0.303	33.577
16	EPIRUBICIN	GLYCINE	-8.932	0.874	9.806	-0.109	0.188	0.297	33.017
17	ASPARTIC ACID	DOXORUBICIN	-10.242	-0.605	9.637	-0.109	0.186	0.295	32.667
18	GLUTAMIC ACID	EPIRUBICIN	-10.044	-1.235	8.809	-0.084	0.187	0.271	32.505
19	GLUTAMIC ACID	DAUNORUBICIN	-10.044	-1.293	8.751	-0.084	0.188	0.272	32.173
20	NORAADRENALINE	DOXORUBICIN	-9.152	-0.605	8.547	-0.083	0.186	0.269	31.772
21	DAUNORUBICIN	SEROTONINE	-8.955	-0.129	8.826	-0.137	0.141	0.278	31.747
22	DOXORUBICIN	GLUTAMIC ACID	-9.299	0.537	9.836	-0.115	0.197	0.312	31.527
23	DOXORUBICIN	ASPARTIC ACID	-9.299	0.516	9.816	-0.115	0.198	0.313	31.359
24	DOXORUBICIN	DOPAMINA	-9.299	0.199	9.498	-0.115	0.189	0.304	31.244
25	DAUNORUBICIN	GABA	-8.955	0.939	9.894	-0.137	0.180	0.317	31.210
26	EPIRUBICIN	GLUTAMIC ACID	-8.932	0.537	9.469	-0.109	0.197	0.306	30.943
27	EPIRUBICIN	ASPARTIC ACID	-8.932	0.516	9.448	-0.109	0.198	0.307	30.774
28	EPIRUBICIN	DOPAMINA	-8.932	0.199	9.130	-0.109	0.189	0.298	30.639
29	ASPARTIC ACID	EPIRUBICIN	-10.242	-1.235	9.006	-0.109	0.187	0.296	30.427
30	DAUNORUBICIN	GLYCINE	-8.955	0.874	9.829	-0.137	0.188	0.325	30.245
31	ASPARTIC ACID	DAUNORUBICIN	-10.242	-1.293	8.949	-0.109	0.188	0.297	30.130
32	DOXORUBICIN	ADRENALIN	-9.299	0.092	9.391	-0.115	0.198	0.313	30.003
33	GLYCINE	DOXORUBICIN	-9.853	-0.605	9.248	-0.126	0.186	0.312	29.641
34	EPIRUBICIN	ADRENALIN	-8.932	0.092	9.023	-0.109	0.198	0.307	29.392
35	NORAADRENALINE	EPIRUBICIN	-9.152	-1.235	7.916	-0.083	0.187	0.270	29.320
36	DOPAMINE	DOXORUBICIN	-8.868	-0.605	8.263	-0.098	0.186	0.284	29.094
37	NORAADRENALINE	DAUNORUBICIN	-9.152	-1.293	7.859	-0.083	0.188	0.271	28.998
38**	DOXORUBICIN	DOXORUBICIN	-9.299	-0.605	8.694	-0.115	0.186	0.301	28.885
39	DAUNORUBICIN	GLUTAMIC ACID	-8.955	0.537	9.492	-0.137	0.197	0.334	28.420
40	DAUNORUBICIN	ASPARTIC ACID	-8.955	0.516	9.471	-0.137	0.198	0.335	28.272
41	EPIRUBICIN	DOXORUBICIN	-8.932	-0.605	8.327	-0.109	0.186	0.295	28.226
42	DAUNORUBICIN	DOPAMINA	-8.955	0.199	9.154	-0.137	0.189	0.326	28.079
43	ADRENALIN	DOXORUBICIN	-8.998	-0.605	8.393	-0.117	0.186	0.303	27.701
44	GLYCINE	EPIRUBICIN	-9.853	-1.235	8.618	-0.126	0.187	0.313	27.532
45	GABA	DOXORUBICIN	-9.562	-0.605	8.957	-0.140	0.186	0.326	27.474
46	GLYCINE	DAUNORUBICIN	-9.853	-1.293	8.560	-0.126	0.188	0.314	27.260
47	DAUNORUBICIN	ADRENALIN	-8.955	0.092	9.047	-0.137	0.198	0.335	27.005
48	DOPAMINE	EPIRUBICIN	-8.868	-1.235	7.632	-0.098	0.187	0.285	26.780
49	DOXORUBICIN	EPIRUBICIN	-9.299	-1.235	8.064	-0.115	0.187	0.302	26.702

50	DOPAMINE	DAUNORUBICIN	-8.868	-1.293	7.575	-0.098	0.188	0.286	26.484
51	DOXORUBICIN	DAUNORUBICIN	-9.299	-1.293	8.006	-0.115	0.188	0.303	26.423
52**	EPIRUBICIN	EPIRUBICIN	-8.932	-1.235	7.696	-0.109	0.187	0.296	26.000
53	DAUNORUBICIN	DOXORUBICIN	-8.955	-0.605	8.350	-0.137	0.186	0.323	25.851
54	EPIRUBICIN	DAUNORUBICIN	-8.932	-1.293	7.638	-0.109	0.188	0.297	25.718
55	ADRENALIN	EPIRUBICIN	-8.998	-1.235	7.763	-0.117	0.187	0.304	25.536
56	GABA	EPIRUBICIN	-9.562	-1.235	8.326	-0.140	0.187	0.327	25.462
57	ADRENALIN	DAUNORUBICIN	-8.998	-1.293	7.705	-0.117	0.188	0.305	25.263
58	GABA	DAUNORUBICIN	-9.562	-1.293	8.268	-0.140	0.188	0.328	25.208
59	SEROTONINE	DOXORUBICIN	-8.948	-0.605	8.343	-0.145	0.186	0.331	25.207
60	DAUNORUBICIN	EPIRUBICIN	-8.955	-1.235	7.720	-0.137	0.187	0.324	23.826
61**	DAUNORUBICIN	DAUNORUBICIN	-8.955	-1.293	7.662	-0.137	0.188	0.325	23.575
62	SEROTONINE	EPIRUBICIN	-8.948	-1.235	7.713	-0.145	0.187	0.332	23.232
63	SEROTONINE	DAUNORUBICIN	-8.948	-1.293	7.655	-0.145	0.188	0.333	22.988

** The drugs that interact with NTs. These interactions mark the limits for electron transfer. All the interactions below them have a high probability that they can be carried out.

4. CONCLUSIONS

We studied the interactions between NTs and three ACys.

We found that the interactions NTs vs. ACys have a very similar pattern in all of them.

The ACys always oxidize the NTs.

We found that SEROTONINE is the most affected of the NTs that were studied.

Our findings coincide with the medical literature of the side effects of these three drugs when used to treat any disease.

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