WORLD JOURNAL OF PHARMACEUTICAL RESEARCH
SJIF Impact Factor 8.084
Volume 9, Issue 1, 378-388. Research Article ISSN 2277– 7105

QUANTUM CHEMICAL ANALYSIS OF THE INTERACTIONS BETWEEN INOSITOL AND THE 20 ESSENTIAL AMINO ACIDS

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Article Received on
09 Nov. 2019,

Revised on 29 Nov. 2019,
Accepted on 19 Dec. 2019,

DOI: 10.20959/wjpr20201-16522

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ABSTRACT

In recent years, many researchers have studied the effect of Inositol and some of its derivatives. These studies have been done on cancer cells and other diseases. The results indicate that there are no significant effects on mitochondrial metabolic activity. In this way, it is known that the total protein profile does not show an alteration with the treatment of Inositol and some derivatives. The objective of this research work was to analyze the chemical-quantum interactions between Inositol and the 20 essential Amino Acids (AAs) using the ETC theory of quantum chemistry. The Hyperchem quantum simulator was used to calculate the quantum variables corresponding to the theory. The calculations were grouped into two main areas: a) Pure substances, b) Cross bands. The results indicate that the Inositol is safe for ingestion in humans. There are only two dangerous interactions, Arg: Inositol and His: Inositol. In these two interactions, Inositol oxidizes these two AAs with a medium probability. We conclude that Inositol is a safe drug for feeding patients. We recommend that it be administered in appropriate doses. High doses could severely affect the patient by their side reactions with the two AAs Arg and His.

KEYWORD: Inositol, amino acids, quantum chemistry. Arginine, Histidine.

INTRODUCTION

Inositol and its derivatives

Researchers analyzed the efficacy of inositol with a genetic desire. They found no scientific evidence that the use of inositol and its isomers significantly increases pregnancy rates in women with a genetic desire.[1,2]; however, myoinositol, in combination with D-chiro-inositol, shows a positive effect in the treatment of patients with the polycystic ovarian

syndrome. This research concludes that this combination of drugs improves serum androgen levels and regulates menstrual cycles. This improvement and regulation may contribute to increased fertility in patients with polycystic ovary syndrome.[3-5]

Regarding the effect of the degradation of calcium and inositol phospholipids on signal transduction, it is indicated that the decomposition of the inositol phospholipid appears to have a signal for transmembrane control of cellular functions and proliferation. This phenomenon is achieved through the activation of protein kinase C. The stimulation of receptors that produce cyclic AMP inhibits the breakdown of inositol phospholipid and blocks the activation of protein kinase C in many tissues. Phorbol esters tumor promoters, can substitute for diacylglycerol and permanently activate protein kinase C independently of the feedback control by cyclic AMP when intercalated into cell membranes.[6-8]

The Cytotoxic study of Inositol Hexaphosphate in the HeLa cell line reports that IP6 has a concentration-dependent cytotoxic effect by altering the cytoskeleton and the cell membrane. The effect of IP6 on HeLa cells shows the depolymerization of microfilaments (cytoskeleton). As a result of this depolymerization, the loss of monolayer formation and rounding of the cells is shown. However, these cells do not lose their adhesion. With exposure to the concentration of 25mg / mL of IP6, the cell begins to lose extracellular communication and its characteristic morphology. There are no apparent changes in the nucleus.[9] Researchers tell us that phosphatidylinositol lipids control critical biological processes. The ability to track the production and localization of these compounds in cells is vital to elucidate their complex roles.[10] By the results obtained by other research postulates that myoinositol affects the supply of transplacental lipids to the fetus in a proposed intervention for gestational diabetes. It is reported that the administration of myoinositol supplements may alter the physiology of placental lipids with unknown clinical consequences.[11]

The effects of InsP6 and InsP5 on the human bone osteosarcoma cell line suggest that these drugs affect endocytosis. Subsequently, this involvement leads to more considerable lysosomal degradation of the swallowed material. Understanding the effects of IPs on human cells is vital to understand the inositol signaling pathways and can lead to the discovery of new anticancer compounds.[12]

The effect of inositol hexaphosphate (ip6) on cancer cells was studied. The results indicate that IP6 has no significant effect on mitochondrial metabolic activity. However, concentration-dependent alteration in cell viability was observed. The total protein profile does not show an alteration on the cancer cells, and the cell nucleus remains intact independent of the concentration of IP6. In contrast, at high concentrations of IP6, the cytoskeleton presents cellular damage. Other studies are necessary to evaluate the antioxidant effect of IP6.[13]

Among other investigations, exposure to air pollution and vehicular traffic has been linked to symptoms of childhood anxiety and in turn, to significant increases in myoinositol. Neuroimaging in patients with anxiety disorders indicates altered neurochemistry. Deregulation of metabolites in the brain and symptoms of generalized anxiety were found among healthy children. This exposure can cause atypical excitatory neurotransmission and glial inflammatory responses. This phenomenon leads to an increase in metabolite levels and subsequent anxiety symptoms.[14]

Amino acids

On the other hand, proteins are polymers of AAs (AA), with nitrogen as the fundamental component. The metabolic balance between intake / synthesis and degradation / loss exists physiologically. Protein synthesis and muscle hypertrophy are promoted by the action of insulin-like growth factor 1 driven by activity and subsequent induction of autocrine and paracrine activities. These are counteracted by the breakdown of proteins through the ubiquitin-proteasome pathway. Oxidative stress and catabolic hormonal increase during critical illness tip the balance towards net protein catabolism, with increased hepatic gluconeogenesis, urea-genesis and AA profile in disordered plasma. Protein catabolism translates into early and severe muscle wasting in critical patients, especially with multi-organ failure.[15]

Quantum Chemistry

In recent years, quantum chemistry has occupied an essential place in the prediction of molecular interactions, both for chemical reactions and for solutions. A new theory was presented to calculate the coefficient of electron transfer between molecules. Theory essence is to calculate how many times an electron or electronic cloud needs its electrostatic potential to jump from the HOMO of one molecule to the LUMO of another molecule. This calculated value is called electron transfer coefficient (dimensionless) (ETC). This concept of ETC is

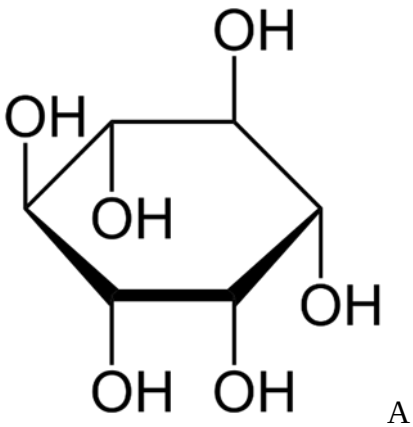
similar to electronic impedance. There is evidence that this theory is consistent with laboratory experiments, both in current literature and in historical literature.[16-23]

Seeing the need to use quantum chemistry, we state the objective of this research work as: Analyze the chemical-quantum interactions between inositol and AAs using the ETC theory. The purpose of this analysis is to test hypotheses that are stated above as state of the art. One of the most exciting hypotheses tells us that "The total protein profile does not show an alteration on the cancer cells and the cell nucleus remains intact independent of the concentration of IP6". In contrast, at "high concentrations of IP6, the cytoskeleton has cellular damage." These authors tell us that other studies are necessary to "evaluate the antioxidant effect of IP6".[13]

MATERIAL AND METHODS

The Hyperchem simulator was used to perform quantum calculations. These calculations are based on the theory of the electron transfer coefficient (ETC) published in other articles. The same author has already announced the database. In this database, it shows the ETC of twenty AA.[16-23]

RESULTS AND DISCUSSIONS



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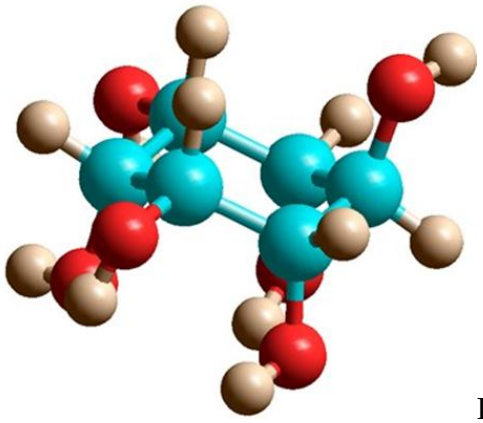

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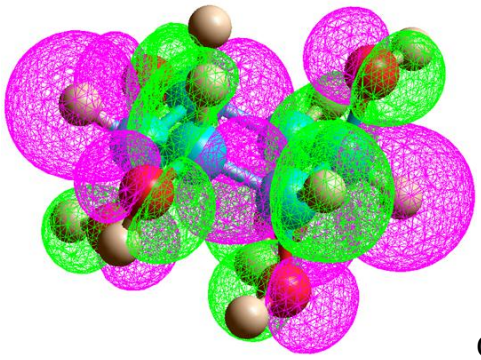

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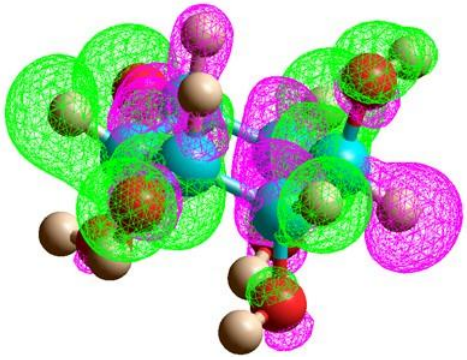

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Fig. 1: Estructura del inositol. A) Fórmula de Howart. B) Fórmula simple. C) HOMO. D) LUMO.

Figure 1: Shows four images of the inositol. In this figure, we can see the simulated images for HOMO and LUMO. The HOMO-LUMO difference makes us think that this substance forms spherical conglomerates or grape clusters.

Table 1: Cross-band analysis of AAs and inositol.

No.	Reducing agent	Oxidizin agent	HOMO	LUMO	BG	E-	E+	EP	ETC
1	Inositol	Val	-10.767	0.931	11.698	-0.101	0.109	0.210	55.704
2	Inositol	Leu	-10.767	0.922	11.689	-0.101	0.130	0.231	50.600
3	Inositol	Ala	-10.767	0.749	11.516	-0.101	0.132	0.233	49.424
4	Inositol	Phe	-10.767	0.283	11.050	-0.101	0.127	0.228	48.464
5	Inositol	Inositol	-10.767	2.366	13.133	-0.101	0.181	0.282	46.570
6	Val	Val	-9.914	0.931	10.845	-0.131	0.109	0.240	45.188
7	Inositol	Gly	-10.767	0.902	11.668	-0.101	0.159	0.260	44.878
8	Inositol	Cys	-10.767	-0.236	10.531	-0.101	0.140	0.241	43.697
9	Glu	Inositol	-10.374	2.366	12.740	-0.111	0.181	0.292	43.631
10	Ser	Inositol	-10.156	2.366	12.523	-0.108	0.181	0.289	43.331
11	Asp	Inositol	-10.370	2.366	12.736	-0.118	0.181	0.299	42.595
12	Inositol	Trp	-10.767	0.133	10.899	-0.101	0.155	0.256	42.575
13	Ala	Ala	-9.879	0.749	10.628	-0.124	0.132	0.256	41.515
14	Inositol	His	-10.767	0.503	11.270	-0.101	0.171	0.272	41.433
15	Leu	Leu	-9.645	0.922	10.567	-0.126	0.130	0.256	41.279
16	Gln	Inositol	-10.023	2.366	12.389	-0.124	0.181	0.305	40.620
17	Inositol	Ile	-10.767	0.972	11.738	-0.101	0.188	0.289	40.617
18	Thr	Inositol	-9.896	2.366	12.263	-0.123	0.181	0.304	40.337
19	Asn	Inositol	-9.929	2.366	12.295	-0.125	0.181	0.306	40.180
20	Ala	Inositol	-9.879	2.366	12.245	-0.124	0.181	0.305	40.147
21	Inositol	Thr	-10.767	0.832	11.599	-0.101	0.191	0.292	39.721
22	Ile	Inositol	-9.872	2.366	12.238	-0.128	0.181	0.309	39.606
23	Inositol	Pro	-10.767	0.792	11.559	-0.101	0.191	0.292	39.584
24	Inositol	Lys	-10.767	0.943	11.709	-0.101	0.195	0.296	39.559
25	Val	Inositol	-9.914	2.366	12.280	-0.131	0.181	0.312	39.359
26	Inositol	Gln	-10.767	0.755	11.521	-0.101	0.192	0.293	39.322
27	Leu	Inositol	-9.645	2.366	12.011	-0.126	0.181	0.307	39.125
28	Phe	Phe	-9.553	0.283	9.836	-0.126	0.127	0.253	38.879
29	Phe	Inositol	-9.553	2.366	11.919	-0.126	0.181	0.307	38.825
30	Inositol	Asn	-10.767	0.644	11.411	-0.101	0.193	0.294	38.812
31	Cys	Inositol	-9.639	2.366	12.005	-0.129	0.181	0.310	38.726
32	Lys	Inositol	-9.521	2.366	11.887	-0.127	0.181	0.308	38.593
33	Gly	Inositol	-9.902	2.366	12.269	-0.137	0.181	0.318	38.580
34	Pro	Inositol	-9.447	2.366	11.813	-0.128	0.181	0.309	38.229
35	Inositol	Ser	-10.767	0.565	11.331	-0.101	0.198	0.299	37.898
36	Inositol	Arg	-10.767	0.558	11.325	-0.101	0.199	0.300	37.748
37	Inositol	Tyr	-10.767	0.293	11.059	-0.101	0.193	0.294	37.616

38	Tyr	Inositol	-9.056	2.366	11.422	-0.123	0.181	0.304	37.573
39	Inositol	Met	-10.767	0.145	10.912	-0.101	0.192	0.293	37.241
40	Inositol	Glu	-10.767	0.438	11.205	-0.101	0.201	0.302	37.102
41	Inositol	Asp	-10.767	0.420	11.187	-0.101	0.204	0.305	36.678
42	Gly	Gly	-9.902	0.902	10.804	-0.137	0.159	0.296	36.500
43	Trp	Inositol	-8.299	2.366	10.665	-0.112	0.181	0.293	36.398
44	Met	Inositol	-9.062	2.366	11.428	-0.134	0.181	0.315	36.280
45	Ser	Ser	-10.156	0.565	10.721	-0.108	0.198	0.306	35.037
46	Cys	Cys	-9.639	-0.236	9.403	-0.129	0.140	0.269	34.956
47	Glu	Glu	-10.374	0.438	10.812	-0.111	0.201	0.312	34.655
48	Ile	Ile	-9.872	0.972	10.844	-0.128	0.188	0.316	34.316
49	Thr	Thr	-9.896	0.832	10.728	-0.123	0.191	0.314	34.167
50	Gln	Gln	-10.023	0.755	10.778	-0.124	0.192	0.316	34.108
51	Asp	Asp	-10.370	0.420	10.790	-0.118	0.204	0.322	33.509
52	**Arg*	*Inositol*	*-9.176*	*2.366*	*11.542*	*-0.165*	*0.181*	*0.346*	*33.359*
53	**His*	*Inositol*	*-9.307*	*2.366*	*11.674*	*-0.169*	*0.181*	*0.350*	*33.353*
54	Asn	Asn	-9.929	0.644	10.573	-0.125	0.193	0.318	33.249
55	Lys	Lys	-9.521	0.943	10.463	-0.127	0.195	0.322	32.495
56	Pro	Pro	-9.447	0.792	10.238	-0.128	0.191	0.319	32.095
57	Trp	Trp	-8.299	0.133	8.431	-0.112	0.155	0.267	31.577
58	Tyr	Tyr	-9.056	0.293	9.349	-0.123	0.193	0.316	29.584
59	His	His	-9.307	0.503	9.811	-0.169	0.171	0.340	28.855
60	Met	Met	-9.062	0.145	9.207	-0.134	0.192	0.326	28.243
61	Arg	Arg	-9.176	0.558	9.734	-0.165	0.199	0.364	26.742
** Inositol as oxidant of His and Arg. Interactions 52 and 53, respectively.*									

Table 1 shows (ETCs) the oxidation-reduction simulations of the 20 AAs vs. inositol. Interactions 54-61 shows us that these eight AAs are very stable, little affected by inositol. This stability can be deduced due to the minimum action law (bottom of the well). Interactions 45-50 also show stability as pure substances of these other six AAs. The rest of the pure AA interactions are shown a little more unstable.

The important thing about this table is that the two interactions marked with asterisks show inositol as an oxidizing agent of His and Arg, respectively.

In humans, Arg is converted in the body into a chemical called nitric oxide. Nitric oxide causes blood vessels to dilate and thus improves blood flow; It also stimulates the release of growth hormone and insulin. In medicine, this AA is indicated to treat cardiac alterations and reduce blood pressure.

His is vital for our organism since its decarboxylation allows its transformation into histamine. In combination with growth hormone and other AAs, it contributes to the repair of cardiovascular tissue. In the central nervous system, it is synthesized and released by neurons

and used as a neuromodulator. The deficiency of this AA can cause hearing problems. It is also vital in the maintenance of the myelin sheaths that surround the neuronal axons. It is also necessary both for the production of red and white blood cells in the blood, protects the body from radiation damage, and reduces blood pressure.

It follows that inositol can affect the functioning of both His and Arg, respectively.

Not complying with this deduction of the involvement of inositol as an oxidizing agent of both His and Arg, we made the calculations of the individual quantum wells (fig. 2-3). Here it is shown in the figure that the affectation has a high average probability.

Dotted lines represent bottoms of the wells of the ETCs of each of the pure substances of the AAs.

The green dot represents the bottom of the Inositol interaction as well as a reducing or antioxidant agent.

The red dot indicates the bottom of the Inositol interaction as well as an oxidizing agent.

The difference between the interactions of both AAs vs. Inositol as an oxidant is negligible. With this, it is said that both AAs are affected in the same proportion.

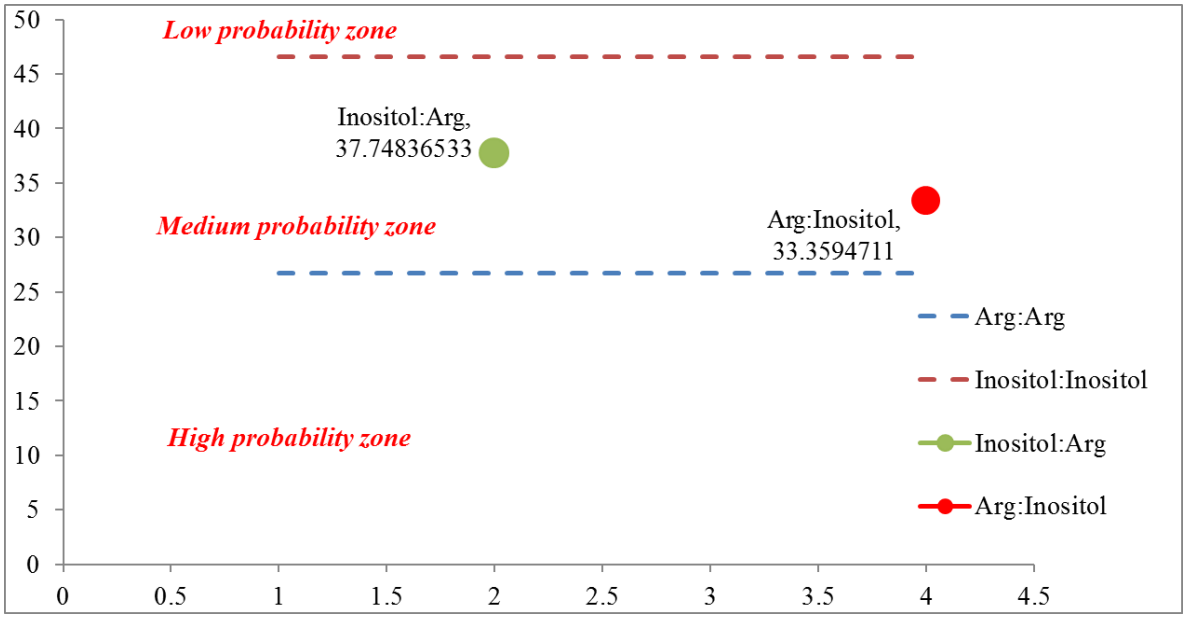

Fig. 2: Quantum well-showing inositol as an oxidant of the AA Arg.

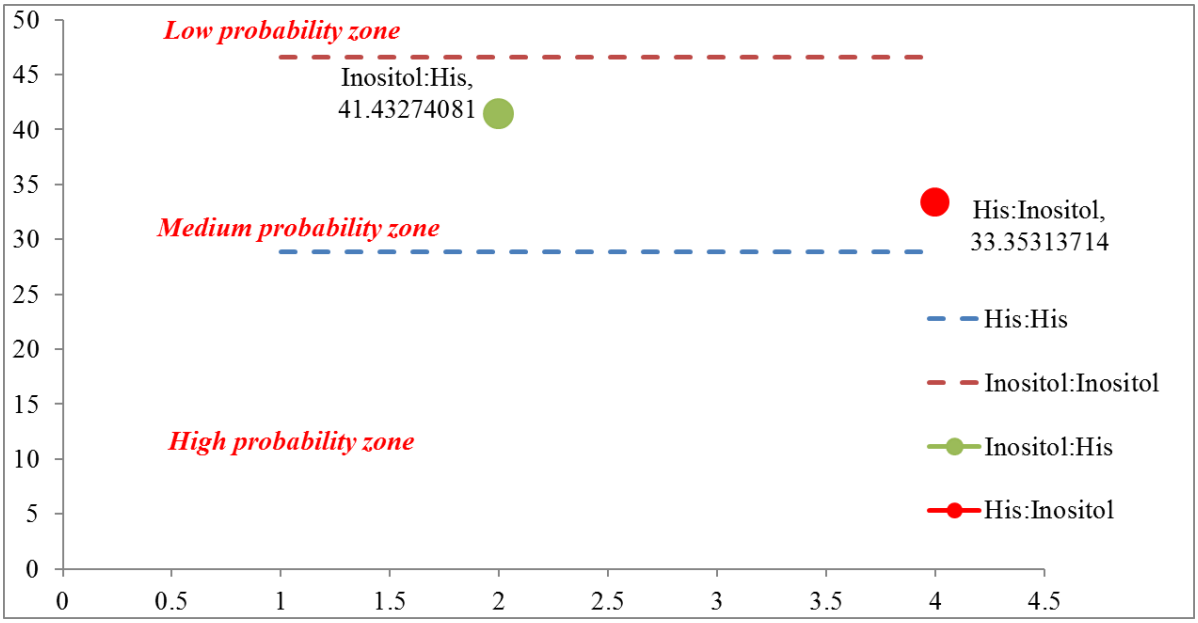

Fig. 3: Quantum well-showing inositol as an oxidant of the AA His.

CONCLUSIONS

We find that:

1. Inositol does not significantly affect AAs. For this reason, it should not have severe side effects.
2. The two AAs that interact with cross bands are Arg and His.
3. The involvement of Inositol to these two AAs can give secondary reactions in the circulatory system, such as:

A) Arg does not become nitric oxide.

B) Do not improve blood flow.

C) Do not stimulate the release of growth hormone and insulin.

D) His does not transform into histamine.

E) His contributes to the repair of cardiovascular tissue.

F) It cannot be used as a neuromodulator.

G) The patient has hearing problems.

H) There are problems with the maintenance of the myelin sheaths that surround the neuronal axons.

I) There are problems with the production of red blood cells as targets in the blood.

J) There are problems with protecting the body from radiation damage.

K) There are problems with blood pressure reduction.

The good news we find is that:

1. The interactions of these two AAs are of medium probability.
2. As a precaution, dosages should be taken care of.
3. These side effects will be carried out with very high dosages.

ACKNOWLEDGMENT

"To our parents. An example of tenacity and hard work."

REFERENCES

1. Fauser BC, Tarlatzis BC, Rebar RW, Legro RS, et al.: Consensus on women's health aspects of polycystic ovary syndrome (PCOS): the Amsterdam ESHRE/ASRM-Sponsored 3rd PCOS Consensus Workshop Group., 2012 Jan; 97(1): 28-38.e25. Epub 2011 Dec 6.
2. Aubuchon M, Legro RS.: Polycystic ovary syndrome: current infertility management. Clin Obstet Gynecol, 2011 Dec; 54(4): 675-84.
3. Azziz R, Marin C, Hoq L, Badamgarav E, Song P. Health care-related economic burden of the polycystic ovary syndrome during the reproductive life span. The Journal of Clinical Endocrinology and Metabolism, 2005; 90(8): 46508.
4. Carmina E, Lobo RA. Polycystic ovary syndrome (PCOS): arguably the most common endocrinopathy is associated with significant morbidity in women. The Journal of Clinical Endocrinology and Metabolism, 1999; 84(6): 1897-9.
5. Carmina E, Rosato F, Janni A, Rizzo M, Longo RA. Extensive clinical experience: relative prevalence of different androgen excess disorders in 950 women referred because of clinical hyperandrogenism. The Journal of Clinical Endocrinology and Metabolism, 2006; 91(1): 2-6.
6. Berridge MJ. (1981) Mol. Cell. Endocrinol, 24; 115–140.
7. Castagna M, Takai Y, Kaibuchi K., Sano K., Kikkawa U. and Nishizuka Y. (1982) J. Biol. Chem., 257: 7847–7851.
8. Graff, G., Stephenson, J.H., Glass, D.B., Haddox, M.K. and Goldberg, N.D. (1978) J. Biol. Chem., 253: 7662–7676.
9. Abulkalam M. Shamsuddin, I. V. (1997). IP6: a Novel Anti-cancer Agent. Elsevier, 343-354.

10. American Cáncer Society, I. (2014). Cáncer de origen primario desconocido. Atlanta, Estados Unidos. American Cancer Society, I. (2015). Métodos complementarios y alternativos para la atención del cáncer.
11. Ricks TJ, Cassilly CD, Carr AJ, Alves DS, Alam S, Tscherch K., ... & Reynolds TB. (2019). Labeling of Phosphatidylinositol Lipid Products in Cells through Metabolic Engineering by Using a Clickable myo-Inositol Probe. Chem Bio Chem, 20(2): 172-180.
12. Watkins OC, Islam MO, Selvam P, Pillai RA, Cazenave-Gassiot A, Bendt AK., ... & Chan SY. (2019). Myo-inositol alters 13C-labeled fatty acid metabolism in human placental explants. Journal of Endocrinology, 1(aop).
13. Degrood, M., Tuescher, J., Mosimann, S., & Golsteyn, R. M. (2019). Investigation of myo-inositol Phosphates on Human Cells by Phenotypic Cell-Based Assays.
14. Murray, M., Birdsall, T., Pizzorno, J. E., & Reilly, P. (2002). La curación del cáncer. (pp 181). American Cancer Society. (2016). Cancer Facts & Figures.
15. Brunst, K. J., Ryan, P. H., Altaye, M., Yolton, K., Maloney, T., Beckwith, T., ... & Cecil, K. M. (2019). Myo-inositol mediates the effects of traffic-related air pollution on generalized anxiety symptoms at age 12 years. Environmental research, 175: 71-78.
16. Chua, H. R., & Puthucheary, Z. A. (2019). Amino Acid Turnover, Protein Metabolism, and Nitrogen Balance in Acute Kidney Injury. In Critical Care Nephrology (pp. 434-442). Content Repository Only!
17. González-Pérez, M. (2017). Quantum Theory of the Electron Transfer Coefficient. International Journal of Advanced Engineering, Management and Science, 3(10).
18. Perez, M. G., Barrera, F. A. G., Diaz, J. F. M., Torres, M. G., & Oglesby, J. M. L. (2014). Theoretical calculation of electron transfer coefficient for predicting the flow of electrons by PM3, using 20 amino acids and nicotine. European Scientific Journal, 10(27).
19. Olmos, NL., Sánchez CD. C. P., Ramírez, M. A., Soria, R., Mioni, L. C., & Perez, M. G. (2018). Quantum chemical analysis of ethanol and its interaction with amino acids and dipeptides (carnosine). World Journal of Pharmacy and Pharmaceutical Sciences, 7(10): 199-208.
20. González-Pérez, MG., Soria, V. R., & Mioni, L. C. (2019). Demonstration of the Formation of the Caffeine-Dichloromethane-water Emulsion using Quantum Chemistry. International Journal of Advanced Engineering, Management and Science, 4(11).
21. García-Aguilar, K., Herrera-Cantú, I., Pedraza-Gress, E., Flores-Gonzalez, L. A., Aparicio-Razo, M., Sánchez-Parada, O., ... & González-Pérez, M. (2018). Quantic Analysis of Formation of a Biomaterial of Latex, Retinol, and Chitosan for Biomedical

Applications. International Journal of Advanced Engineering, Management and Science, 4(1).

22. González-Pérez, M., Gonzalez-Martinez, D., González-Martínez, EL., Pacheco-Bautista, D., & Medel-Rojas, A. (2018). Theoretical-Chemical-Quantum Analisys of Sarin Neurotoxicity. World Journal of Pharmacy and Pharmaceutical Sciences, 7(5): 173-180.
23. Torres-Contreras, Y, Iglesias-Arruti, CE, Moreno-Hernández M, Nayeli Contreras-Contreras, Ana Karen Cid-Rosiles, Manuel Gonzalez-Perez: chemical-quantum analysis of the biological activity of bioactive dipeptids for the possible treatment of diabetes. World Journal of Pharmaceutical Research, 06/2019; 8(8): 1-10.
24. Erick Pedraza-Gress, Karina García-Aguilar, Regina Escamilla-Violante, Manuel Gonzalez-Perez: Quantum chemical analysis of the effect of sucralose (splenda) interactions on nitrogenous bases (DNA and RNA). Global Journal of Engineering Science and Research Management, 04/2019; 6(4): 10-17., DOI:10.5281/zenodo.2639261.