Electronic Supplementary Material (ESI) for Chemistry Education Research and Practice.


# APPENDIX 1. COMPUTATIONAL CHEMISTRY INTO THE CHEMISTRY CURRICULUM – A SUMMARY OF EARLIER RESEARCH

| Type of Implementation | Course | Place | RGCCS* | Title of Article | Ref. |
|---|---|---|---|---|---|
| Into chemistry curriculum | Computational Chemistry / Organic Chemistry Laboratory | University of North Carolina at Wilmington, USA | PCModel, HyperChem, Alchemy2000, Spartan, Gaussian94, Spreadsheet Excel. | Integration of Computational Chemistry into the Chemistry Curriculum | (Martin, 1998) |
| Into chemistry curriculum | Computational Chemistry | University of Chicago, USA | Mathematica, Insight II suite of programs, GAMESS | Computational Chemistry in the Undergraduate Chemistry Curriculum: Development of a Comprehensive Course Formula | (Gasyna and Rice, 1999) |
| Into chemistry curriculum | General Chemistry Laboratories/ Organic Chemistry Laboratories/ Inorganic Chemistry Course and Laboratory/ Analytical Chemistry Course/ Biochemistry Courses | Humboldt State University, Arcata, California, USA | PC Spartan Pro, Gaussian 98W and GaussView, Mathematica, Jaguar, GAMESS, AIMPRO | Molecular Modeling and Computational Chemistry at Humboldt State University | (Paselk and Zoellner, 2002) |
| Into the chemical engineering curriculum | Computational Chemistry | Worcester Polytechnic Institute, Worcester Massachusetts, USA | Gaussian98, gOpenMol, MATLAB, WebMO 4.1 | Incorporating Computational Chemistry into the Chemical Engineering Curriculum | (Wilcox, 2006) |
| Into chemistry curriculum | Laboratory course | Kenyon College, Gambier, Ohio, USA | Berkeley Madonna | An Educational Approach to Computationally Modeling Dynamical Systems | (Chodroff*, et al.*, 2009) |
| Into pharmaceutical science (medicinal chemistry) undergraduate program | Medicinal Chemistry Course | Monash University, (Parkville Campus) | HyperChem | Conformational Analysis of Drug Molecules: A Practical Exercise in the Medicinal Chemistry Course | (Yuriev*, et al.*, 2009) |
| Into course curriculum | Physical Chemistry | University of Washington, Seattle, Washington, USA | Spartan Student Edition, GAMESS, Ghemical | Integrating Computational Chemistry into the Physical Chemistry Curriculum | (Johnson and Engel, 2011) |
| Into upper-level course for engineering students | Quantum Chemistry and Spectroscopy for Engineering Undergraduate Students | Northwestern University, Evanston, Illinois, USA | NUITNS (https://nanohub.org), GAMESS, MacMolPlt, Molden | Northwestern University Initiative for Teaching NanoSciences (NUITNS): An Approach for Teaching Computational Chemistry to Engineering Undergraduate Students | (Simeon*, et al.*, 2011) |
| Into Physical chemistry curriculum | Physical chemistry | University of Washington, Seattle, USA | Spartan | Integrating Computational Chemistry into the Physical Chemistry Curriculum | (Johnson and Engel, 2011) |
| Into course curriculum | Physical Chemistry Laboratory | Grand Valley State University, Allendale, Michigan, USA | Gaussian, The Molecular Modeling Workbook for Organic Chemistry | Integrating Computational Chemistry into the Physical Chemistry Laboratory Curriculum: A Wet Lab/Dry | (Karpen*, et al.*, 2004) |

| | | | | | |
|---|---|---|---|---|---|
| | | | | Lab Approach | |
| Into course syllabus | Organic Chemistry Laboratory | Randolph-Macon College, Ashland, Virginia, USA | PC Spartan Plus | An Integrated Molecular Modeling and Melting Point Experiment for the Organic Chemistry Laboratory | (Poon*, et al.*, 1999) |
| Into course syllabus | Organic chemistry course | Poznan University of Medical Sciences | ALOGPS 2.1 | Prediction of log P: ALOGPS Application in Medicinal Chemistry Education | (Kujawski*, et al.*, 2011) |
| Into course syllabus | Organic chemistry laboratory | Boise State University, USA | Spartan | Modeling $S_N2$ and E2 Reaction Pathways and Other Computational Exercises in the Undergraduate Organic Chemistry Laboratory | (Csizmar*, et al.*, 2013) |
| Into course syllabus | Physical Organic Chemistry | University of Waterloo, Waterloo, Ontario, Canada | Gaussina09 | Theoretical Hammett Plot for the Gas-Phase Ionization of Benzoic Acid versus Phenol: A Computational Chemistry Lab Exercise | (Ziegler, 2013) |
| Into course syllabus | Physical organic chemistry | University of Waterloo, Canada | Gaussian09 | Theoretical Hammett Plot for the Gas-Phase Ionization of Benzoic Acid versus Phenol: A Computational Chemistry Lab Exercise | (Ziegler, 2013) |
| Into course syllabus | Physical chemistry laboratory | Sonoma State University, California, USA | Web-based software, Avogdro, MacMolPlt, GAMESS | Web-Based Job Submission Interface for the GAMESS Computational Chemistry Program | (Perri and Weber, 2014) |
| Into course syllabus | Physical Chemistry | Beloit College, Beloit, Wisconsin, USA | Excel | Introduction to Computational Chemistry: Teaching Hü ckel Molecular Orbital Theory Using an Excel Workbook for Matrix Diagonalization | (Litofsky and Viswanathan, 2015) |
| Into course syllabus | Physical Chemistry | Azusa Pacific University, Azusa, California, USA | Spartan10, Gaussian09 | Walsh Diagrams: Molecular Orbital and Structure Computational Chemistry Exercise for Physical Chemistry | (Miller and Ellison, 2015) |
| Into course syllabus | Organic Chemistry Laboratory | University of Wisconsin, Madison, Wisconsin, USA | Gaussian 09, PSI4, GAMESS | Integration of Computational Chemistry into the Undergraduate Organic Chemistry Laboratory Curriculum | (Esselman and Hill, 2016) |
| Into course syllabus | Physical Chemistry Laboratory | Alma College, Alma, Michigan, USA | Spartan Student, Spartan 14, Maple, Excel | Empirically Corrected Electronic Structure Calculations Applied to the Enthalpy of Combustion Physical Chemistry Laboratory | (Mazzuca*, et al.*, 2019) |

| | | | | | |
|---|---|---|---|---|---|
| Into course syllabus | Analytical Chemistry | Taylor University, Upland, Indiana, USA | WebMO, PSI4 | Integrated TGA, FTIR, and Computational Laboratory Experiment | (Pemberton, *et al.*, 2019) |
| Proposed computational exercises | Proposed computational exercises for inorganic chemistry classes | Chemistry Department, Petroleum Institute, Abu Dhabi, United Arab Emirates | WebMO, MOPAC, GAMESS | Testing and Extending VSEPR with WebMO and MOPAC or GAMESS | (McNaught, 2011) |
| A proposed computational experiment | Physical chemistry | Università degli Studi di Padova, Italy | Molden, Visual Molecular Dynamics (VMD), NAMD, Gaussian 09, Octave | Computational Study of Environmental Effects on Torsional Free Energy Surface of N-Acetyl-N′-methyl-l-alanylamide Dipeptide | (Carlotto and Zerbetto, 2013) |
| Research | Computational-theoretical chemistry laboratory adaptation to blind and visually impaired students interested in research | University of California—Davis, USA | Open Babel, Gaussian03 | Applied Computational Chemistry for the Blind and Visually Impaired | (Wedler, *et al.*, 2012) |

**RGCCS: Research-Grade Computational Chemistry Software*

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# APPENDIX 2. THE PBL SCENARIO

## SCENARIO: REQUIREMENT OF THE WORLD HEALTH ORGANIZATION ON CHAGAS DISEASE

Chagas disease is an endemic disease in 21 countries of the American continent, from the southern United States to southern Argentina, especially in countries, such as Mexico, Central America and South America. It is estimated that in the region, about 100 million people are at risk of becoming infected, about 8 million infected, with 56,000 new cases per year for all forms of transmission, generating 12,000 deaths annually. (Gascon*, et al.*, 2010; Guadalupe Pérez*, et al.*, 2011; Montgomery*, et al.*, 2014) Valdez et al. (2009) showed the potential of β-carboline derivatives (β-CD) like anti-chagasics against three forms of the protozoan parasite that caused this disease: *Trypanosoma cruzi* (*T. cruzi*), by mean of *in vitro* and *in vivo* studies. (Valdez*, et al.*, 2009) Currently, research on Chagas disease has led to the identification of the enzyme Trypanothione Reductase (TR) (Protein Data Bank Code 1AOG, http://www.rcsb.org/pdb/home/home.do) like an Interesting therapeutic target in the treatment of this disease.

On the other hands, today exist enough information of scientific interest available into databases such as PubChem (https://www.ncbi.nlm.nih.gov/pccompound), which can be employed for the identification of commercially available compounds as potential future drugs. The rapid generation of virtual libraries with miles of molecular structures and also the computational evaluation of these molecular structures against a particular therapeutic target is a widely used technology for the identification of potential enzymatic inhibitors (Muddassar*, et al.*, 2010; Badrinarayan and Sastry, 2012; Di-wu*, et al.*, 2012; Shi*, et al.*, 2012). In this sense, the concept of a drug-like compound developed by Lipinski (1997) has been widely used, which indicates that drugs administered orally frequently are in areas of chemical space defined by a limited number of molecular properties being grouped into the known Rule of Five (RO5) (Lipinski, et al., 1997).

Rodríguez et al. (2017) showed that the virtual screening method represents a strategy for identifying potential TR inhibitors. In this research, nine potential TR inhibitors were discovered among commercially available β-CD. This result shows that β-carboline scaffolds can be a good starting point for further development of TR inhibitor (Rodríguez-Becerra*, et al.*, 2017). In this sense, the World Health Organization (WHO) has considered that to focus the search of commercial β-CD using like a substructure the β-CD: (Figure 1), can be an interesting starting point for identifying new potential TR inhibitors. Moreover, for this challenger WHO has considered that its research group has knowledge into area of: database searching, application different filtering steps to reduce the number of candidate compounds, 3DMV and identification of potential enzymatic inhibitors with base on intermolecular forces. These are computational capacities necessaries to identify a new potential TR inhibitor.

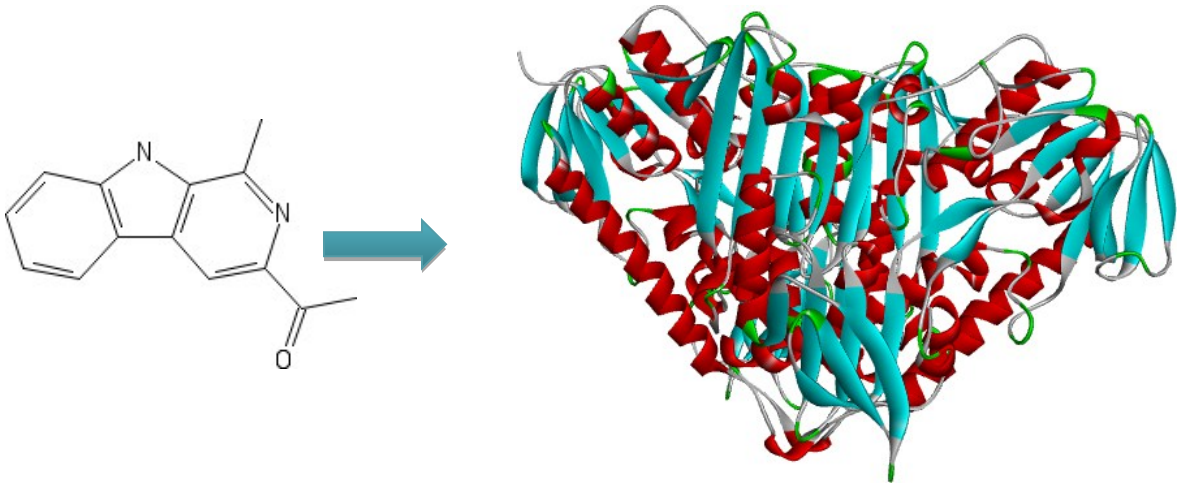


**Figure 1.** Molecular and representation of TR.

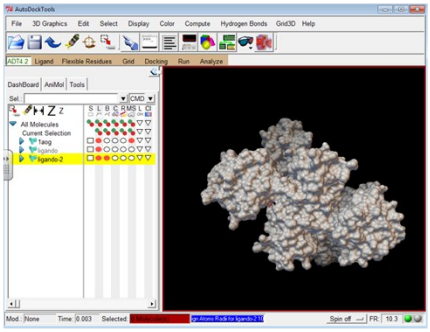
## DIGITAL RESOURCES:


1. https://www.ncbi.nlm.nih.gov/pccompound
2. http://www.rcsb.org/pdb/home/home.do
3. http://autodock.scripps.edu/
4. http://autodock.scripps.edu/faqs-help/tutorial/using-autodock-4-with-autodocktools/2012_ADTtut.pdf
5. https://pymol.org/
6. Morris G. M., Goodsell D. S., Huey R. and Olson A. J., (1996), Distributed automated docking of flexible ligands to proteins: Parallel applications of AutoDock 2.4, J. Comput.-Aided Mol. Des., 10, 293-304.

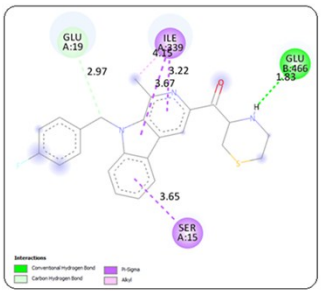
# APPENDIX 3. EXAMPLES OF THE DATA AND POSTERS PRODUCED IN THE ECC MODULE

1

Beginning

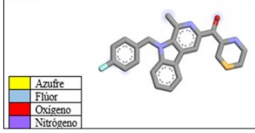


2

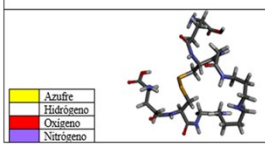



Results

Analysis and conclusions

| *Molécula DBC8* | *Conformero* | *Energía final intermolecular / kcal × mol⁻¹* |
|---|---|---|
|  | 1 | -9.06 |
| | 2 | -9.03 |
| | 3 | -9.07 |
| | 4 | -8.56 |
| | 5 | -8.46 |
| | 6 | -9.09 |
| | 7 | -8.25 |
| | 8 | -8.43 |
| | 9 | -8.48 |
| | 10 | -8.64 |

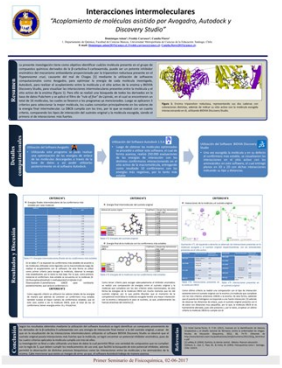


| *Molécula del sustrato original* | *Conformero* | *Energía final intermolecular / kcal × mol⁻¹* |
|---|---|---|
|  | 1 | -6.55 |
| | 2 | -6.17 |
| | 3 | -7.35 |
| | 4 | -5.48 |
| | 5 | -6.91 |
| | 6 | -8.15 |
| | 7 | -4.79 |
| | 8 | -7.32 |
| | 9 | -7.38 |
| | 10 | -6.27 |



3

Poster Presentations




4

# APPENDIX 4. INTERVIEW QUESTIONS

**Table**. Questions employed into the focus group with pre-service chemistry teacher.

| | |
|---|---|
| 1 | What do you think about the Computational Chemistry Module implemented in the subject matter of Intermolecular Forces into Physical Chemistry I course? |
| 2 | What content did you find easier to learn? Why do you think this was easier for you? |
| 3 | What content did you find most difficult to learn? Why do you think this was more difficult for you? |
| 4 | What scientific skills did you think has developed or strengthened? |
| 5 | What activities or tasks into Module do you think helped in development or strengthened of your scientific skills? |
| 6 | What activities or tasks into Module do you think contributed less in development or strengthening of your scientific skills? |
| 7 | What strengths do you think presents Research-Grade Computational Chemical Software (RGCCS) integration to the learning of chemistry? Why? |
| 8 | What weaknesses do you think presents RGCCS integration to the learning of chemistry? Why? |
| 9 | How do you evaluate your own process of learning disciplinary contents with this module? Why? |
| 10 | How do you evaluate your own process of development of scientific skills with this module? Why? |
| 11 | What do you think about the problem-based learning methodology used in this module? |
| 12 | In relation to the time that you normally use in tasks outside the classroom, what do you think about the time outside the classroom employed to make the tasks related with this module? |
| 13 | What kind of future forecast do you make of this learning experience in your future job like a chemistry teacher? |