TD-DFT Study of Chalcones with Potential Pharmacological Activity against Alzheimer's Disease

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INTRODUCTION

One of the main diseases of the 21st century is Alzheimer's disease, a neurodegenerative disorder, which commonly attacks patients more than 65 years old. Its main feature is the progressive cell death of neurons, causing its main symptom: the loss of memory and cognitive ability of the patient. There is no cure for Alzheimer's disease, and its main method of palliative treatment is based on the cholinergic hypothesis, acting on the activity of acetylcholinesterase (AChE). By inhibiting this activity, the cholinergic deficit decreases.[1] Among the compounds developed to act as an AChE inhibitor are several chalcones, some that have already been used as prototypes for new drugs. With that in mind, our research group has synthesized and studied some new chalcones in order to observe the action of these new molecules face up to the action of AChE. The experimental work of synthesis and biological activity is being finalized and will be published soon. Here, we discussed about theoretical properties,[1] specifically, UV-vis theoretical calculations based on Time Dependent Density Functional Theory (TD-DFT). This theoretical study will supply us in important aspects related to the photophysical behavior of these new compounds.

METHODS

Figure 1 shows the chalcones studied in this work. [2]

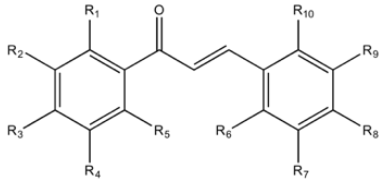

Figure 1: Representation of the base structure of Chalcones studied, with the following substituents: **R1:** H, NH_2; **R2:** H, NH_2; **R3:** H, NH_2, NO_2; **R4:** H, NH_2; **R5:** H, NH_2; **R6:** H, OH; **R7:** H, OCH_3; **R8:** H, OH, NO_2, OCH_3, CH_2CH_3, CH_3, OCH_2CH_3; **R9:** H, OH, OCH_3; **R10:** H, OH.

Based on similar structures, previously studied, all theoretical calculations were performed in G09 program suite at the TD-PBE1PBE/6-311+G(2d,p) //CAM-B3LYP/6-311G(d,p) level.

RESULTS AND DISCUSSION

The calculated data, such as the orbital energies and the theoretical UV-Vis spectrum for one of the 33 chalcones studied, are arranged in Figure 2, as well as the electronic densities of its HOMO and LUMO orbitals and electron density difference between the S_1 and S_0 states.

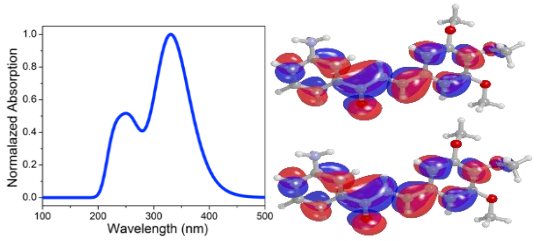

Figure 2: Electronic density of LUMO (top – right) and HOMO (bottom – right), and the theoretical UV-Vis spectrum (oscillator force vs. wavelength – to the left) at TD-PBE1PBE/6-311+G(2d,p)//CAM-B3LYP/6-311G(d,p) level.

In all molecules derivatives, HOMO orbitals is concentrated on the methoxyphenyl side, whereas the LUMO are more distributed, but clearly show a tendency towards the conjugated C=C–C=O moiety of the structure (Michael system). Also, as depicted in Figure 2, both HOMO and LUMO are of π type.

CONCLUSIONS

Theoretical results indicate an efficiency of the intramolecular charge transfer (ICT) process to stabilize the dye in the excited state.

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[2] MOTA, A. A. R. et al. Theoretical Photophysics (DFT) of Fluorescent Benzothiadiazole Probes. Revista Virtual de Química, v. 7, n. 1, 2015.