MOLECULAR MODELING OF YM348 AND SB242084 COMPOUNDS WITH O 5-HT$_{2C}$ RECEPTOR

Madson S. do Nascimento, Moacyr Comar Jr., Kelson M.T. Oliveira, Saulo L. da Silva

Depto de Química – ICE - Universidade Federal do Amazonas (UFAM), CEP 69077-000, Manaus, AM, Brazil

The serotonin receptors (5-HT$_{2C}$) are involved in many physiological processes as the anxiety control, depression and appetite fluctuation. The comprehension about interactions of agonists (YM348) and antagonist (SB2484) compounds with 5-HT$_{2C}$ receptors will provide new knowledge to aid on developing new and more effective pharmacs. Initially the YM348 and SB242084 compounds were subdued to a conformational analysis. The final structures utilized in the electronic, molecular and energetic analysis were optimized through the Density Functional Theory (DFT) B3LYP/6-31G* until an energy gradient of 0,001kcal/mol. The properties studied were: HOMO and LUMO energies, Mulliken electronegativity, total and electronic energies, net charge over atoms, polarizability, refractivity, dipolar moment, log P, area and volume. Both compounds showed planar structures, being it possible to occupy the same space onto a receptor, however the physic-chemical characteristics of both are very different. The antagonist show lower energies, total and electronic and also lower Mulliken electronegativity. Additionally the antagonist has higher HOMO energy, dipolar moment, refractivity, polarizability and log P. These factors possibly induce the antagonist (SB242084) to form a more stable complex with the receptor than the one formed by the agonist (YM348). FAPEAM / CNPq.