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Structure-Activity Relationship of Tacrine and Analogous Against Alzheimer´s disease

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Abstract: Alzheimer's disease is a chronic neurodegenerative disease responsible for almost 70% of all case of dementia. Its cause is not yet completely understood, but 70% of the risk is believed to be genetic with many genes involved. Each year, thousands of new cases are reported around the world and this number is estimated to be three times higher in 2050[1]. Currently, there are some medicines that can control the Alzheimer's disease symptoms but its healing is not yet available[2]. Discovery new drugs that can better control the evolution of that disease is a very active research field in chemistry [3]. Here, we report a structure activity relationship study of a set of tacrine compounds and their analogues with activity against Alzheimer's disease [3]. Density functional theory with the exchange-correlation functional B3LYP[4] and the basis set 6-31G(d) were used to calculate the molecular descriptors. The principal component analysis technique [5] was employed to discriminate the compounds in active (1 a 8, 11 e 13) and inactive groups (9,10 e 12). The results show that five descriptors are required for complete discrimination of the compounds (Figure 1): HOMO and LUMO energies, angle between atoms 1, 6 and 16 (Figure 2), atomic partial charge on atom 4(Figure 2) and dipole moment. These findings can be used in the modeling of new tacrine analogues that have enhanced activities against Alzheimer's disease.

Key-words: Alzheimer, Tacrine and analogues, DFT, PCA.

Figure 1 PC1_PC2 score plot

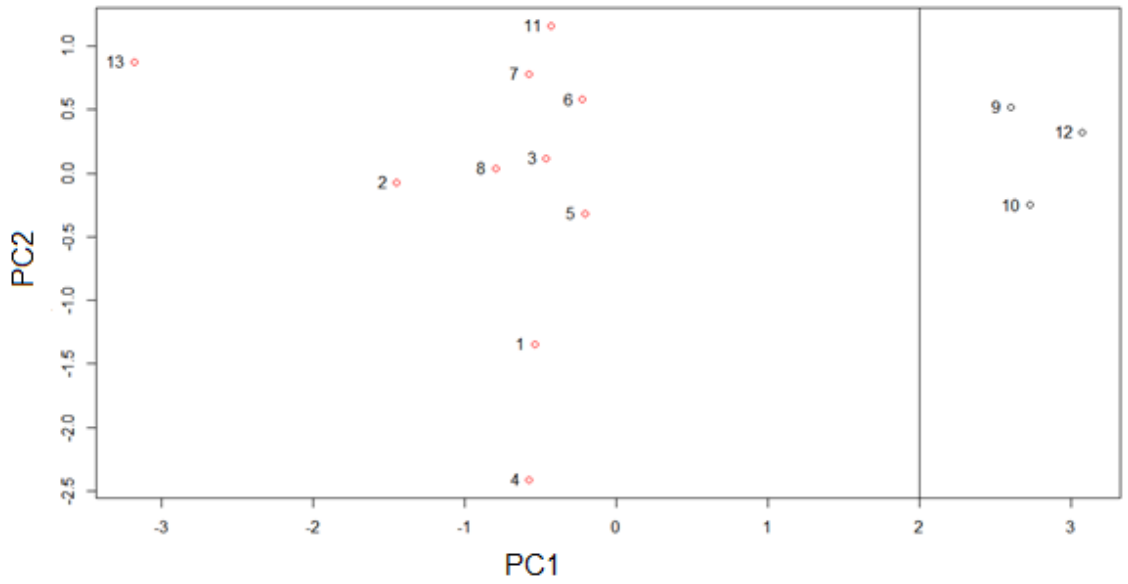
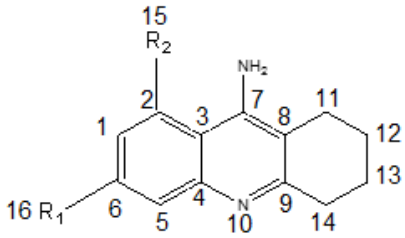


Figure 2 Molecular structure basic numbered for labelling atoms



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