Structural Basis for Anti-Cancer Activity Of A Novel Metoxiflavona Derivative From *Strychnos Pseudoquina*

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The Cerrado biome is considered one of the 34 hotspots worldwide, due to its high degree of endemism and the reduction of its native area due to the expansion agribusiness[1]. The characteristics of altitude, soil, and relief of the Cerrado favor the occurrence of secondary metabolites such as flavonoids, which have relevant pharmacological properties, and can be potentiated due to the differentiation of functional groups in their basic structure. In this sense, the compound 5,7,3',4'-tetrahydroxy-3-methoxyflavone (FLV), extracted from the plant *Strychnos pseudoquina*, was comprehensively characterized by spectroscopic techniques (^{1}H and ^{13}C nuclear magnetic resonance), thermal methods (thermogravimetric analysis, differential scanning calorimetry), and single crystal X-ray diffraction (Figure1). The topological analysis was carried out through the Hirshfeld surface in order to get insights on supramolecular architecture and structure-activity relationship. The FLV compound ($C_{19}H_{12}D_6O_8$) was crystallized in the monoclinic space group $P2_1/n$ with one solvent acetone-d6 in the asymmetric unit (Final R indices: R_1 = 0.0701, wR_2 = 0.1909; *Goof* = 1.065). The electronic study was performed using the density functional theory at level M062X/6-311++G(d,p), generating frontier molecular orbitals and molecular electrostatic potential map. The lowest unoccupied molecular orbital appears as a π antibonding and it is localized on the pyrone ring with an energy value of 21.19 kcal/mol. The energy gap is 210.44 kcal/mol indicating that FLV is chemically stable. Finally, in vitro cytotoxicity assays were performed on MDA-MB-231, A549, A2780cis, MCF-10A and MRC-5 cell lines, and both qualitative and quantitative models relating FLV structure to biological activity were undertaken. Acknowledgments: This research was supported by the Fundação de Amparo à Pesquisa do Estado de Goiás (FAPEG), Conselho Nacional de Desenvolvimento Científico e Tecnológico (CNPq) and High Performance Computing Center of the Universidade Estadual de Goiás.

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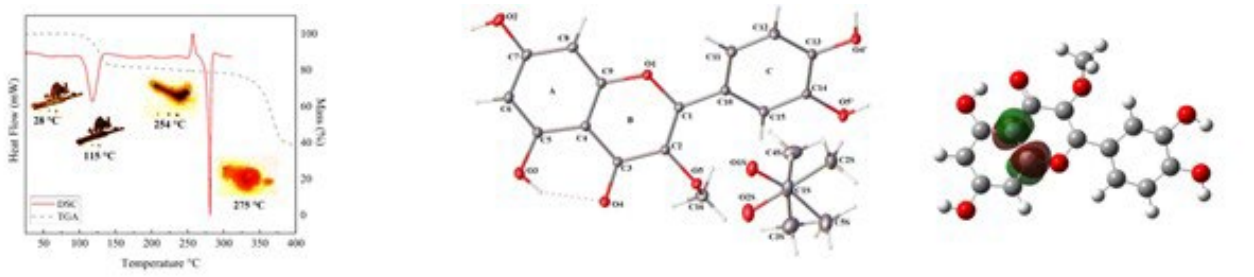

Figure 1. (a) DSC and TGA curves with Hot-Stage microscopy agreement; (b) Ortep diagram with 50% probability ellipsoid with the atomic numbering scheme; (c) The lowest unoccupied molecular orbital with the isovalue of 0.05 atomic units showing π pure *antibonding* orbital.

Figure 1