Synthesis, crystal and molecular structure, vibrational spectroscopic, DFT study and activity evaluation of 4-(2-chlorobenzyl)-1-(4-hydroxy -3-((4-hydroxypiperidin-1-yl)methyl-5-methoxyphenyl)-[1,2,4] triazolo[4,3-a]quinazolin-5(4H)-one

Qingmei Wu[1], Wenjun Ye[1], Qian Guo[1], Tianhui Liao[1], Weike Liao[2], chunshen Zhao[1], Huifang Chai[3], and Zhixu Zhou[1]

[1]Guizhou University
[2]Guizhou Medical University
[3]Guizhou University Of Traditional Chinese Medicine

February 19, 2021

Abstract

In current work, we have firstly synthesized 4-(2-chlorobenzyl)-1-(4-hydroxy-3- ((4-hydroxypiperidin-1-yl)methyl)-5-methoxyphenyl)-[1,2,4]triazolo[4,3-a]quinazolin-5(4H)-one (1) by ring-opening, cyclization, substitution, doamine condensation and Mannich reactions. The structural properties of the title compound 1 were explored using spectroscopy (1H NMR, 13C NMR, MS and FT-IR) and X-ray crystallography method. The single-crystal structure confirmed by X-ray diffraction was consistent with the molecular structure optimized by density functional theory (DFT) calculation at B3LYP/6-311G (2d, p) level of theory. The geometrical parameters, molecular electrostatic potential (MEP) and frontier molecular orbital (FMO) analysis were performed by DFT using the B3LYP/6-311G (2d, p) method. Molecular docking has shown favorable interaction between the title compound 1 and SHP2 protein. The inhibitory activity of target compound 1 on SHP2 protein at 10 μM is better than the reference compound (SHP244).

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