

## Documents

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**Synthesis, spectroscopic characterizations, TD/DFT calculations, colorimetric metal ions, and molecular docking studies of a novel 3-acetylpyridine 2-hydroxyphenyl thiosemicarbazone**  
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**Abstract**

A novel thiosemicarbazone scaffold, namely 3-acetylpyridine-2-hydroxyphenyl thiosemicarbazone (3APHT), which contains  $\pi$ -conjugated heterocyclic and phenyl rings, was successfully synthesized and characterized experimentally and theoretically. Through TD/DFT calculations, it was found that the new compound has 14 signals in <sup>13</sup>CNMR spectroscopy, 96 types of vibrations for vibration analysis, and  $n-\pi^*$  and  $\pi-\pi^*$  electronic transitions that lead to an 87.12 % HOMO-LUMO excitation. The vibrations follow 3N-6 degrees of freedom for a non-linear compound. Based on the global reactivity parameter and other results, it has been shown that 3APHT has potential applications in metal ion detection and as an inhibitor for the overexpressed receptor of breast cancer caused by copper ions pollution. The novel APHT was optimized as a colorimetric metal ions recognition using UV-Vis analysis. Suitable conditions for 3APHT to act as a colorimetric metal ion recognition was detected in DMSO/water (8:2 v/v, pH 7). The change of test strips from colorless to yellowish revealed the presence of Cu<sup>2+</sup> ions in the water. The selectivity toward the Cu<sup>2+</sup> ion did not interfere with other metal ions. The potential of 3APHT to inhibit the upregulation of apoptotic genes caused by copper ions in BCL-2 family proteins—the main cause of breast cancer—was determined using an in-silico approach. The results showed strong binding of 3APHT with BCL-2, BCL-W, MCL-1, and ER- $\alpha$  through hydrogen bonds and electrostatic interactions at -6.35, -6.31, -8.05, and -7.05 kcal/mol, respectively. The physicochemical through ADME analysis showed that the compound has a structure that presents good absorption properties, therefore permeability across the cell membrane, and good theoretical oral bioavailability. © 2024

**Author Keywords**

3-acetylpyridine 2-hydroxyphenyl thiosemicarbazone; Colorimetric metal ions; Global reactivity parameters; Molecular docking; Spectroscopy; TD/DFT

**Index Keywords**

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