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## Synthesis, Characterization, Antibacterial Screening and DFT (Density Functional Theory) Studies of Thiosemicarbazide Ligands and Its Copper(II) and Nickel(II) Complexes

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**Background:** Thiosemicarbazide ligands are known to have positive impact on microbial activity and has become one of the alternatives to combat the multi-drug resistance bacteria. Thiosemicarbazide can coordinate with the metal ions because the presence of sulphur atom (C=S) and nitrogen atom (C=N) which will contribute their lone electron pairs. From the coordination, they depict unique antibacterial properties which will interact with the bacterial cells. Thiosemicarbazide shows activities against *Escherichia coli* and *Staphylococcus aureus* by in-vitro screening.

**Methods:** The ligands were synthesized via condensation reactions of thiosemicarbazide with various benzaldehydes, resulting in three distinct compounds: 4-hydroxybenzaldehyde (LA), 4-nitrobenzaldehyde (LB), and 4-fluorobenzaldehyde (LC) derivatives. These ligands were then complexed with copper(II) and nickel(II) acetate to form metal complexes with a 1:2 metal-to-ligand ratio. The synthesized ligands and metal complexes were characterized using a range of analytical techniques including UV-Vis, IR, and NMR spectroscopy, as well as elemental analysis. Disk diffusion methods also have been conducted to test the ligands and metal complexes antibacterial capabilities. The DFT studies implemented in this study was using B3YLP 6-31G (d,p) level of theory.

**Results:** Significant peaks in IR spectroscopy for ligands are C=N (1584-1604  $\text{cm}^{-1}$ ) and C=S (1232-1344  $\text{cm}^{-1}$ ). Coordination of ligands with copper(II) and nickel(II) shifted the C=N and C=S bond stretching to lower frequencies ((1582-1588  $\text{cm}^{-1}$  and 1586-1598  $\text{cm}^{-1}$ ). For the UV-Vis, the  $\Pi$ - $\Pi^*$  transition of C=N can be observed at 224, 265 and 233 nm for LA, LB and LC respectively. In NMR spectroscopy, the peak of NH for ligands appears sharp at 11.16-11.58 ppm. The results of antibacterial screening indicate LC have significant antibacterial effect with diameter of inhibition zone of 18 mm against *Streptococcus mutans* (Gram +ve bacteria). Frontier Molecular Orbital (FMO) energy gap of LA, LB and LC are -0.14930, -0.11035, and -0.14605 eV respectively. The small FMO energy gap shows that the ligands are polarized and reactive which affects the ligand's biological activity.

**Conclusion:** In conclusion, this study demonstrates that thiosemicarbazide ligands and their metal complexes hold promise as potential antibacterial agents, especially in the fight against multi-drug resistance bacteria.

**Keywords:** Thiosemicarbazide, copper(II) complexes, nickel(II) complexes, DFT, antibacterial activity

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