Synthesis, Characterization, and Biological Studies of Schiff Base,1-([1,1-biphenyl]-4-yl)-N-(4-bromophenyl) methenamine and N-(4-bromophenyl)-1-(naphthalene-2-yl) methenamine

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Introduction

Schiff bases are condensation products of primary amines with carbonyl compounds; typically prepared using organic solvents with the elimination of water molecules. They have a general formula of $R_1R_2C=NR_3$, where R_1, R_2, and R_3 represent the alkyl/aryl substituents. Schiff bases are widely recognized for their applications in industrial, medicinal, and agricultural fields, exhibiting various biological activities such as antimicrobial, antifungal, antioxidant, and insecticidal properties. Among the widely used organic compounds, Schiff bases are used as intermediates in organic synthesis, catalysts, pigments, dyes, and as polymer stabilizers. This study aims to synthesize and characterize Schiff base compounds with minimal or no side effects.

Materials and methods

Synthesis of 1-([1,1-biphenyl]-4-yl)-N-(4-bromophenyl) methenamine (BBM) and N-(4-bromophenyl)-1-(napthalen-2-yl) methenamine (BNM). The condensation reaction between 4-biphenyl carboxaldehyde,2-naphtaldehyde, and 4-bromine aniline at room temperature yielded a milky white solid product (BBM) and a silver-white solid product (BNM), respectively. These compounds were characterized using UV-visible, FT-IR, melting points, and solubility tests. In vitro antimicrobial tests and physicochemical and pharmacokinetics calculations were performed on the products.

Results and discussion

The reaction yields are 73 and 67% with melting points of 170 and 140°C, respectively. While BBM was insoluble in most polar solvents, including water, BNM demonstrated a contrasting solubility characteristic. However, the two compounds were soluble in diethyl ether, ethyl acetate, benzene, and chloroform. Using Lipinski's RO5, the estimated parameters including molecular weight (MW), lipophilicity (logP), aqueous solubility (logS), topological polar surface area (TPSA), and LD50 revealed that the two compounds have a good bioavailability characteristic in terms of absorption and cellular uptake because of their molecular weights estimated to be 336.23 and 310.19 g/mol for BBM and BNM, respectively. The acceptable molecular weight for active compounds is 500 g/mol, this indicates that BBM and BNM fall below the acceptable threshold. BBM had an estimated LogS value of 6.30, indicating good solubility, and BNM (-5.51) showed poor solubility. The estimated LogP values for BBM and BNM were 5.38 and 4.82, respectively. This indicates good lipophilicity characteristics for BBM in agreement with Lipinski's RO5. BBM and BNM had a uniform TPSA of 12.36$Å^2$, which means their ability to permeate the cells. BBM and BNM have low estimated LD50s and therefore tend to be ingested orally. The antibacterial studies of the ligands showed that they exhibited higher bactericidal activity against Klebsiella sp. and *Escherichia coli.*

Conclusions

This study successfully synthesized a new series of Schiff base ligands,1-([1,1-biphenyl]-4-yl)-N-(4-bromophenyl) methenamine and N-(4-bromophenyl)-1-(naphthalene-2-yl) methenamine. The results of their characterizations showed few violations of the rule of five (RO5). They also possessed antibacterial activities against Klebsiella sp and Escherichia coli with a good MIC and MBC. The compounds are recommended for advanced analytical characterization and in vitro biological activity.

Keywords: Schiff base, Synthesis, Pharmacokinetics, Antibacterial activity