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Synthesis and Preliminary Antibacterial Screening of Salicylaldehyde-3-Aminobenzoic Acid and its Metal Complexes

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ABSTRACT

The synthesis and preliminary antibacterial screening of a novel organic ligand, Salicylaldehyde-3-aminobenzoic acid (SAB), and its metal complexes are reported in this study. SAB was synthesized through a simple condensation reaction between salicylaldehyde and 3-aminobenzoic acid. The complexes were prepared from SAB and salts of Fe^{2+} *and* Ni^{2+}*. Some physical characteristics such as colour and solubility were determined. Preliminary screening was also carried out using the disc diffusion method against a panel of clinically relevant bacterial strains, including Staphylococcus aureus, Streptococcus pyogenes, Eschericha coli and Salmonella typhi. The result indicated that* Fe^{2+}*-SAB and* Ni^{2+}*-SAB showed varying zones of inhibition on the bacteria and exhibited enhanced antibacterial activity when compared to the free ligand. However,* Fe^{2+}*-SAB showed no activity against Streptococcus pyogenes and* Ni^{2+}*-SAB showed no activity against Eschericha coli. This suggests potential applications of* Fe^{2+}*-SAB and* Ni^{2+}*-SAB in the development of new antibacterial agents.*

Keywords: SAB, Schiff bases, Ligands, Metal complexes.

INTRODUCTION

In recent times, there has been a noticeable increase in the morbidity and mortality rates attributed to a variety of diseases and infections [1]. These illnesses are primarily caused by microorganisms or organisms, such as bacteria, leading to the loss of thousands of lives daily, even though conventional drugs and medications are readily available. What's concerning is that these infectious diseases have developed resistance to a broad spectrum of antimicrobial and antiseptic treatments, diminishing the efficacy of these administered drugs [2, 3]. These microorganisms not only affect humans and animals but also have a detrimental impact on our agricultural products. Fortunately, there is a renewed sense of hope in addressing this pressing issue with the emergence of complexes containing Schiff bases [4].

Schiff bases have garnered widespread attention among chemists globally because of their straightforward synthesis and complexation properties [4, 5, 6]. They were originally created by the renowned German chemist and Nobel Prize laureate Hugo Schiff [7]. Schiff bases are ligands that form coordination bonds with metal ions through azomethine nitrogen (-RC=N-) (Figure 1). Typically, they are generated when primary amines undergo condensation reaction with active carbonyl compounds [7]. Essentially, Schiff bases can be viewed as structural counterparts to ketones or aldehydes having C=O (carbonyl group) substituted by C=N-R (imine or azomethine group) [8].

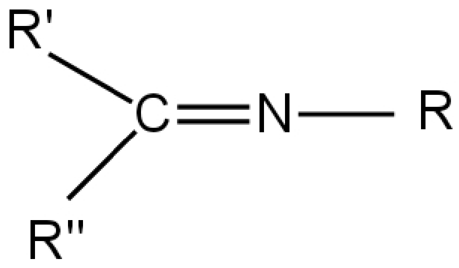


Figure 1: General Structural Formula of Schiff Bases

Schiff base-transition metal complexes are highly versatile and extensively researched systems used as model molecules in various applications, including biological oxygen carriers [6]. These compounds are widespread in living organisms and have uses in organic synthesis, chemical analysis and catalysis, healthcare, pharmaceuticals and emerging innovations. They are used in recent years in both homogeneous and heterogeneous catalytic processes [8] and enzyme preparations [5]. Schiff base coordination complexes exhibit good antifungal, antibacterial, anticancer, anti-inflammatory, analgesic, antianxiety activities, DNA interaction, cytotoxicity and anti-HIV properties [5, 6, 9].

Schiff bases are synthesized by combining two or more distinct compounds. For instance, 2-[(5-styryl-[1,3,4]thiadiazol-2-ylimino)-methyl] is prepared from 3-phenylacrylic acid, thiosemicarbazide, and phosphorus oxychloride [10]. Rauf and colleagues synthesized the Schiff base 1-((3-nitrophenylimino)methyl)naphthalen-2-olate from 2-hydroxynaphthaldehyde and 3-nitroaniline [11]. In the present study, the Schiff base, salicylaldehyde-3-aminobenzoic acid, was synthesized by reacting 3-aminobenzoic acid and salicylaldehyde in an ethyl acetate medium. The Schiff base was individually coordinated with Fe (II) and Ni (II) metal salts to form complexes, and their bactericidal activities were evaluated.

MATERIAL AND METHODS

Materials

The apparatus used include beaker, round bottom flask, funnel and filter paper. The reagents and solvents used include salicylaldehyde, 3-aminobenzoic acid, iron (II) acetate monohydrate, nickel (II) acetate monohydrate, ethanol, methanol, n-hexane and distilled water. The bacteria strains used include *Staphylococcus aureus, Escherichia coli, Streptococcus pyogenes* and *Salmonella typhi.* All chemicals and solvents were purchased and utilized without further purification.

Methods

Synthesis of Ligand

A solution of salicylaldehyde (20 mmol) contained in 15 ml of ethanol in a flask was slowly added to 3-aminobenzoic acid (10 mmol) already dissolved in 10 ml of ethanol in a separate round-bottom flask. On addition of the two solutions, they were stirred for at room temperature for 15 minutes at

400 rpm. The product started to precipitate during this period. The synthetic route for the preparation of the ligand (salicylaldehyde-3-aminobenzoic acid) is depicted in Figure 2.

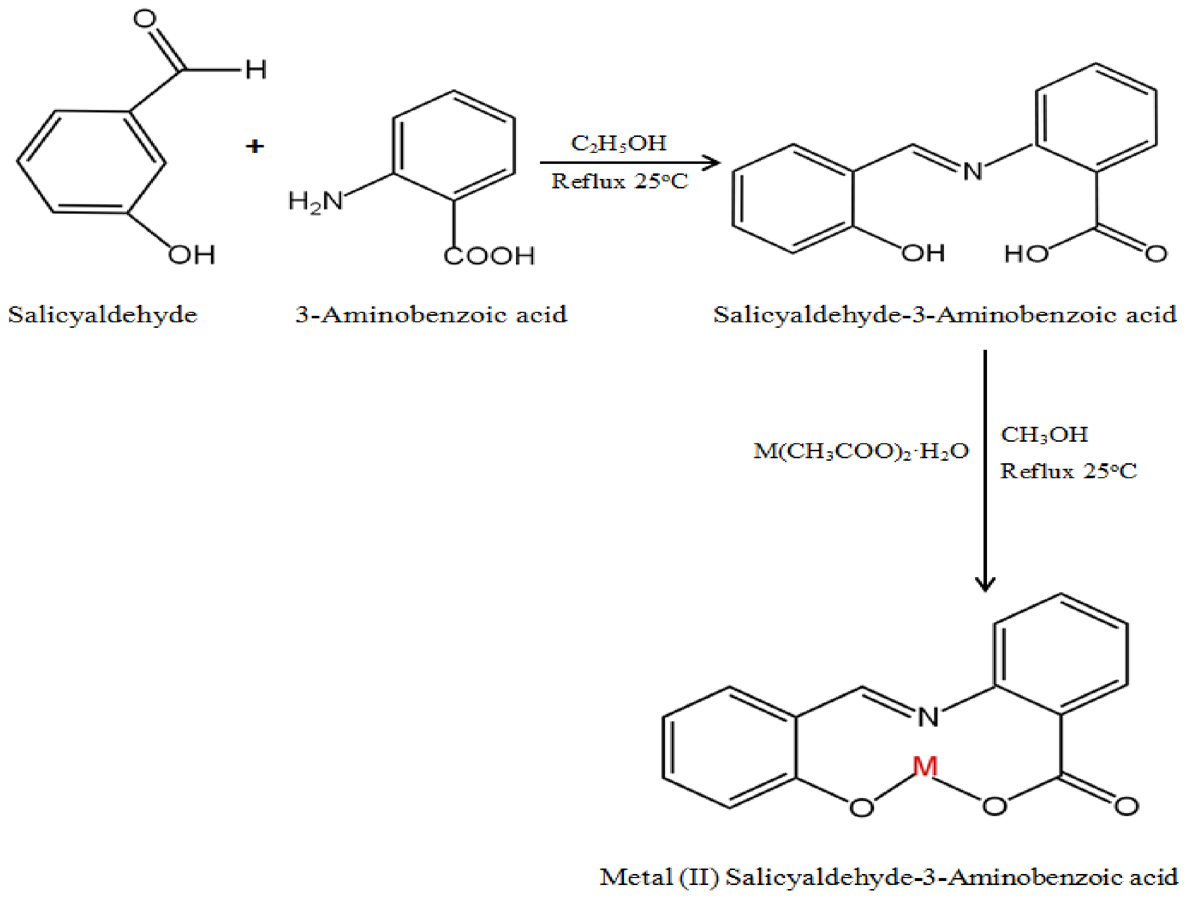
Synthesis of the Metal Complexes

Synthesis of Iron (II) Salicyaldehyde-3-Aminobenzoic acid

Iron (II) acetate monohydrate (1.2 g) was weighed into a beaker containing 20 ml of hot methanol and added slowly to salicyaldehyde-3-aminobenzoic acid (0.5 mmol) while stirring. The reaction mixture was allowed to cool, filtered, and subsequently rinsed extensively with water and methanol. The obtained product consisted of dark green flakes corresponding to the metal complex.

Synthesis of Nickel (II) Salicyaldehyde-3-Aminobenzoic acid

Nickel (II) acetate monohydrate (1.2 g) was weighed into a beaker containing 20 ml of hot methanol and added slowly to salicyaldehyde-3-aminobenzoic acid (0.5 mmol) while stirring. The reaction mixture was allowed to cool, filtered, and subsequently rinsed extensively with water and methanol. The obtained product consisted of dark blue flakes corresponding to the metal complex.



$M(CH_3COO)_2 \cdot H_2O$ = Metal(II)acetate monohydrate

Figure 2. Synthetic Route for the Preparation of Metal Complexes (M = Fe and Ni).

Solubility Test

The solubility of the salicyaldehyde-3-aminobenzoic acid, Fe^{2+}-SAB and Ni^{2+}-SAB were determined in water and some common organic solvents (ethanol, methanol and N-hexane). 2g of the sample were separately measured and dissolved in 10ml of the individual solvent and allowed to dissolve for 10 min [3].

Antibacterial screening

The preliminary antibacterial activity of salicyaldehyde-3-aminobenzoic acid, Fe^{2+}-SAB and Ni^{2+}-SAB was assessed by the agar diffusion method against four bacteria strains: *Staphylococcus aureus, Streptococcus pyogenes, Escherichia coli* and *Salmonella typhi*. The compound (0.01 g) was weighed and dissolved in 10 mL of DMSO. The compound was loaded on a standard sterilized filter paper disc (6.35 mm diameter) and positioned on agar plates inoculated with the respective test microbes. Incubation of the plate was done at 37ºC for 24 h after which the zone of inhibition (mm) was measured by a ruler [3].

RESULTS AND DISCUSSION

Physical Properties of the Compounds

Table 1: Physical Properties of the Compounds

Compounds	Molecular Formula	Molecular Weight (g/mol)	Colour/Texture
SAB	$C_{14}H_{11}NO_3$	241	-
Fe^{2+}-SAB	$Fe[C_{14}H_9NO_3]$	294.85	Dark green flakes
Ni^{2+}-SAB	$Ni[C_{14}H_9NO_3]$	297.69	Dark blue flakes

The complexes had distinct colour and texture. Fe^{2+}-SAB had a dark green colour while Ni^{2+}-SAB was dark blue.

Solubility of the Compounds

Table 2: Solubility of the Compounds

Compounds	Water	Ethanol	Methanol	n-Hexane
SAB	CS	CS	CS	SS
Fe^{2+}-SAB	SS	SS	SS	CS
Ni^{2+}-SAB	CS	CS	CS	SS

Key: CS= Completely soluble**,** NS= Not soluble**,** SS= Slightly soluble

The solubility of a compound in different solvents is a key indicator of its chemical characteristics and potential applications. In Table 2, the solubility of salicyaldehyde-3-aminobenzoic acid, Fe^{2+}-SAB and Ni^{2+}-SAB were evaluated in four solvents: water, ethanol, methanol and n-hexane. SAB demonstrates complete solubility (CS) in polar solvents like ethanol, water, and methanol, in line with its polar nature. However, it shows only slight solubility (SS) in nonpolar n-hexane, underscoring its limited compatibility with nonpolar solvents.

Fe^{2+}-SAB maintains complete solubility (CS) in non-polar solvent (n-Hexane), indicating that the complex retains its solubility in these environments. However, it exhibits slight solubility (SS) in ethanol, water, and methanol, suggesting that the presence of SAB in the complex might influence its solubility in polar solvents. Similarly, Ni^{2+}-SAB displays complete solubility (CS) in polar solvents and slight solubility (SS) in N-hexane, reinforcing its adaptability in both polar and nonpolar environments.

The observed variations in solubility among the SAB, Fe^{2+}-SAB and Ni^{2+}-SAB are primarily due to differences in their chemical structures, polarity, and the effects of complexation, which influence their interactions with solvents of varying polarities [13].

Bactericidal Activity of the Compounds

Table 3: Zones of Inhibition of Bacteria in the Presence of Ligand and Complexes

Compounds	**Zone of Inhibition (mm)**			
	S. aureus	***S. pyogenes***	***E. coli***	***S. typhi***
SAB	1	3	2	3
Fe^{2+}-SAB	NA	5	4	7
Ni^{2+}-SAB	2	NA	7	4

Key: NA = No activity, SAB = Salicylaldehyde-3-Aminobenzoic acid

The presented results (Table 3) show the zone of inhibition, measured in millimeters, for different complexes tested against four distinct bacterial strains: *S. aureus, S. pyogenes, E. coli,* and *S. typhi.* The inhibition zone indicates the area surrounding an antimicrobial agent where bacterial growth is inhibited. From the results for salicylaldehyde-3-aminobenzoic acid (SAB), it is evident that SAB demonstrates varying degrees of effectiveness against the tested bacterial strains. SAB has the smallest zone of inhibition against *S. aureus* (1 mm zone diameter of inhibition), indicating that this bacterium is the least sensitive to the antibiotic. In contrast, SAB has a more pronounced inhibitory effect on *S. pyogenes, E. coli,* and *S. typhi,* with the largest inhibition zone observed for *S. pyogenes* and *S. typhi* (3 mm zone diameter of inhibition).

Fe^{2+}-SAB complex exhibited a notable inhibition zone against *S. pyogenes* (5 mm zone diameter of inhibition), *E. coli* (4 mm zone diameter of inhibition), and *S. typhi* (7 mm zone diameter of inhibition), suggesting its effectiveness in inhibiting the growth of these bacterial strains. However, it is worth noting that this complex did not affect the growth of S. aureus. Notably, the most significant zone of inhibition was observed for *S. typhi*, indicating that the Fe^{2+}-SAB complex is particularly effective against this bacterial strain.

Ni^{2+}-SAB complex inhibitory properties are distinctive. This complex displayed an inhibition zone against *S. aureus, E. coli,* and *S. typhi* but did not have any inhibitory effect on *S. pyogenes.* The most substantial zone of inhibition was observed against *E. coli*, highlighting the effectiveness of the Ni^{2+}-SAB complex against this bacterium. These results illustrate that the effectiveness of these complexes in inhibiting bacterial growth is dependent on the specific bacterial strain being tested. Both the Fe^{2+}-SAB and Ni^{2+}-SAB complexes exhibit antimicrobial properties, albeit with variations in their effectiveness against different bacteria.

The higher activity of the complexes, such as Fe^{2+}-SAB and Ni^{2+}-SAB, compared to salicylaldehyde-3-aminobenzoic acid against specific bacterial strains may be attributed to various factors, including the chelation effect involving metal ions, different mechanisms of action, strain-specific sensitivities, complex stability and solubility, potential synergistic effects with the complex, variations in bacterial uptake mechanisms, and the possibility of certain strains having developed resistance the complex [14, 15]. These factors collectively contribute to the enhanced antimicrobial properties of the complexes against particular bacterial strains and underscore the multifaceted nature of their effectiveness, necessitating further research to comprehensively justify these variations in antimicrobial activity.

CONCLUSION

The synthesis of salicylaldehyde and 3-aminobenzoic acid yielded a ligand, bridging salicylaldehyde and 3-aminobenzoic acid moieties, which subsequently formed metal complexes with iron (Fe) and nickel (Ni) ions. Salicyaldehyde-3-aminobenzoic acid, Fe^{2+}-SAB and Ni^{2+}-SAB were tested for their potential as antimicrobial agents against various bacteria strain. The results indicated varying levels of inhibition, with Fe^{2+}SAB showing no activity against *Streptococcus pyogenes*, and Ni^{2+}SAB showing no activity against *Escherichia coli*. The enhanced antibacterial activity demonstrated by these metal complexes compared to the free ligand suggests their promise as potential candidates for the development of new antibacterial agents. The versatility of Schiff base-transition metal complexes in various biological and chemical applications underscores the significance of this research. Further investigations into the precise mechanisms of their antibacterial activity and optimization of their effectiveness will be essential for advancing their potential utility in the fields of medicine and chemical technology.

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