SYNTHESIS AND *IN-VITRO* STUDY OF SOME TRANSITION METAL COMPLEXES OF NOVEL HETEROCYCLIC SCHIFF BASES AS POTENTIAL ANTI-TUBERCULOSIS AGENTS

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A THESIS SUBMITTED TO THE POSTGRADUATE SCHOOL OF THE UNIVERSITY OF LAGOS IN PARTIAL FULFILMENT OF THE REQUIREMENTS FOR THE AWARD OF DOCTOR OF PHILOSOPHY IN INORGANIC CHEMISTRY

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A Thesis submitted in Fulfilment of the Requirements for the Degree of Doctor of Philosophy (Ph.D.) in the Department of Chemistry, School of Postgraduate Studies, University of Lagos, Lagos, Nigeria.

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CERTIFICATION

This is to certify that the Thesis:

"SYNTHESIS AND *IN-VITRO* STUDY OF SOME TRANSITION METAL COMPLEXES OF NOVEL HETEROCYCLIC SCHIFF BASES AS POTENTIAL ANTI-TUBERCULOSIS AGENTS"

Submitted to the
School of Postgraduate Studies
University of Lagos

For the Award of the degree of
DOCTOR OF PHILOSOPHY (Ph.D)
is a record of original research carried out
by:

DUEKE-EZE, CORDELIA UKAMAKA
In the Department of Chemistry

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DEDICATION

I dedicate this research to my Blessed mother, Our Lady of Perpetual Help for her intercession throughout the period of this programme.

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ABSTRACT

The increasing reports of resistance of *Mycobacterium tuberculosis* (*M.TB*) to the classical anti-tuberculosis drugs pose a challenge to effective control of *M.TB.* This drug resistance has led to renewed interest in the search for new classes of compounds active against *M.TB.* Novel Schiff bases were obtained by the condensation reaction of 2-hydroxybenzaldehyde (salicylaldehyde), 5-nitro-2-hydroxybenzaldehye (5-nitrosalicylaldehyde), 5-bromo-2-hydroxybenzaldehyde (5-bromosalicylaldehyde) and 5-methoxy-2-hydroxybenzaldehyde (5-methoxysalicylaldehyde) with 2-aminopyridine (**L1-L4**), 4-aminopyridine (**L5-L7**) and isonicotinic acid hydrazide (INH) (**L8-L11**). In addition, more INH Schiff bases were obtained by the reaction of 2-pyrrole carboxaldehyde, 2-thiophene carboxaldehyde and INH (**L12-L13**). These Schiff bases were reacted with $CuCl_2.2H_2O$, $NiCl_2.6H_2O$ and $CoCl_2.6H_2O$ to form Cu(II), Ni(II) and Co(II) complexes. The synthesized compounds were evaluated for their *in-vitro* anti-tuberculosis activity against a standard (*M.TB* $H_{37}Rv$) and clinical isolate strains using the proportion method. The compounds were characterized using melting point, infrared (IR), ^{1}H and ^{13}C nuclear magnetic resonance (NMR), electronic absorption, atomic absorption spectroscopy, elemental analyses and conductivity measurements. The physical data revealed that the Schiff bases were obtained in moderate to high yields. Based on the infrared and electronic absorption spectroscopic data, the geometry for the copper complexes of aminopyridines (**L1A-L7A**) and INH (**L8A-L10A**) were deduced to be square planar and octahedral respectively. With few exceptions, most of the nickel and cobalt complexes were octahedral owing to their spectral behavior. The geometries of all the complexes (**L12A-L13C**) containing either the pyrrole or thiophene moiety were deduced to be square planar. The copper complexes had the general formulae $[MLX.H_2O].nH_2O$ (**L1A-L7A** and **L13A**) and $[ML_2].nH_2O$ (**L8A-L12A**), the nickel complexes are of the general formulae $[ML_2.nH_2O].nH_2O$ (**L3B-L5B**), $[ML_2]$ (**L6B**, **L7B, L12B** and **L13B**), $[ML.nH_2O].X.nH_2O$ (**L8B** and **L9B**) and $[MLX.nH_2O].nH_2O$ (**L10B-11B**) and the cobalt complexes had the general formulae $[ML_2.nH_2O].nH_2O$ (**L1C-L7C**), $[ML.nH_2O].X.nH_2O$ (**L8C**) and $[ML_2].nH_2O$ (**L9C, L12C** and **L13C**), (M = metal, L = Schiff base, X = chlorine). The conductivity measurements reveal that all the complexes except **L8B**, **L8C** and **L9B** were non-electrolytes. The synthesized compounds were evaluated for their *in-vitro* anti-tuberculosis activity against *Mycobacterium tuberculosis* $H_{37}Rv$ and a clinical isolate. The anti-tuberculosis activity of most of the Schiff bases increased with the presence of metal ion. The copper and cobalt complexes of the pyrrole and nitro-containing compounds exhibited significant activity when compared with the reference compound (INH). In addition, the cobalt complex having the thiophene moiety showed significant effect on the clinical isolate. These compounds can be considered as a good starting point to develop new novel lead compounds for the management of tuberculosis.