**REVIEW ARTICLE**

# Mixed Ligand Complexes of Trimethoprim: A Review

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**ABSTRACT**

In this research, we highlight the most important research related to the mixed ligand complexes of the drug trimethoprim (TMP), and for the past 7 years where this drug has been used as a chelating ligand and gives stability to the complexes with ions of metal elements where these complexes, prepared and diagnosed, and for some research the bacterial activity was studied against different types of bacteria.

**Keyword:** Bacterial activity, Ligand complexes, Trimethoprim.

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## INTRODUCTION

In the medicine field, biological and chemical processes including antioxidants, water-smoothing, ion exchange resin, photo syntheses in plants, removal of unwanted and risky metals from the electrical components of living organisms, which are also very relevant to environmental chemistry, mixed ligand complexes have an important role to play[1-7] in this subject. Antimicrobial drug production was a big success story in the 20th century.[8] TMP is a wide spectrum Antibiotic in addition to exhibits antiphrastic activities.[9] The use of chelate compounds has received large attention.[10,11] Mixed of TMP and Isoniazid with five transition metal ions were prepared. The complexes are categorized based on IR, melting point, and conductivity measurement. Based on reported papers about the coordination sites are showed through (N- pyrimidine) group of TMP and coordination through the (N- amine) group of Isoniazid.[12] The Ag (I) complexes of TMP and pyrimethamine have been prepared and diagnosed using fourier transform infrared spectroscopy (FTIR), CHN, and UV-Vis spectroscopic analyses. The metal chelates formed 3 and 4 coordinated geometries with ligands as the monodentate molecule bonding to the Ag(I) in every case via the (N-pyrimidine).[13] Two ligand TMP and pyrimethamine with Pt(II) and Pd(II) complexes have been created and characterized via HNMR, UV-vis, FTIR spectroscopic, and CHN. The complexes have been subedited as four coordinated square planar structures.[14] In nutritional ingredients Saccharin is one of the most studied components because it's harmful and it could cause cancer degases.[15] Mixed ligand complexes of Cu(II), Fe(II), Zn(II), Co(II), Ni(II), Hg(II) as well as Cd(II).[16] A novel mixed ligand complexes have been prepared of Mn(II), Co(II), Fe(II), Ni(II), Zn(II), and Cd(II) with Saccharin and L-Valine, all complexes with $[M(Val)_2(Sac)_2]$ formulas.[17]

### Mixed Ligand Complexes for Drug Trimethoprim

The PD(II) along with Pt(II) TMP and pyrimethamine complexes categorized by elementary analyses of UV, FTIR and NMR spectroscopy techniques. The complexes have been composed of four square, 2D coordinate species with dual medicine molecules and dual chlorides or thiocyanate ions. Spectroscopic analyzes verified a coordinating of metallic ions with a pyrimidine nitrogen atom for drugs. The complexes were tested against eight bacterial isolates for their antibacterial activity. They demonstrated diverse behaviors with more enhanced inhibition in the active metal complexes

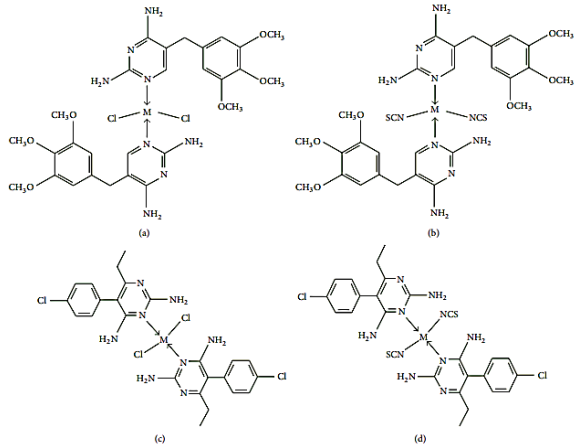

**Figure 1:** Suggested structures of metal complexes

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than TMP or pyrimethamine. In the Pd (II) Pyrimethamine complexes, *P. aeruginosa* and B were unusually inhibitory. The activity of pumilus and no other complexes or drugs against certain bacteria isolates was demonstrated. MIC and MBC results indicate that Pd (II) have been the maximum effective complexes. The structural activity relationship has shown that Pt (II) chloride ion complexes are more active and Pd(II) ion-containing complexes have increased activity than ion chloride ions.[18]

Preparation and characterization for complexes [methyl-βeta-cyclodextrin and hydroxyl propyl-ßeta-cyclodextrin (HBCD)] and TMP inhibitors of bacterial dihydrofolate reductases and cyclodextrines in water solution. MBCD was chosen for the preparation of solid-state incus ion complexes. These complexes were made using various techniques: spray drying, kneading, and freezing drying. The relation was the preparation of physical mixtures. Differential calorimetric scanning, FTIR spectroscopy characterized the preparations by different techniques. TMP's antimicrobial activity has been tested with a system of diffusion, respectively.[19]

The trimethoprim and sulfamethoxazole mixed drug metal (II) complexes were synthesized, distinguished by metal percentages, infrared and electronic spectroscope spectrums, and magnetic moments at room temperatures, melting points, and conductance measures. In the metal test, it was found that [M(HL)(HL)x].nHO is used for the study of the complexes. Here, M= Mn, Co, Ni, Cu, Fe, Zn besides Cl=SO. The magnet moment and electronic spectral information show that the metal complex (II) is magnetically diluted and octahedral. The metal (II) molar conductance in DMSO has confirmed the covalence of all complexes. In-vitro antimicrobial investigations of hydroxyl propyl-ßeta-cyclodextrin, Proteus mirabilis, Bacillus spp, Pseudomonas spp, Streptococcus piogenes, *Staphylococcus aureus* and Candida albicans in these metal (II) complexes, TMP and SMX.[20]

Mixed bivalent complexes Ni(II), Zn(II), Co(II), Cu(II), Cd(II) along with HG(II) have been summarized by frequent determining solubility, melting point, molar conductivity, metal percentage in complexes through FTIR, magnetic susceptibility, based on given data. For bacterial activity, both ligands and metal complexes have been investigated for selected microbe strains (gram +) and (gram -).[21]

The mixed complex L-Proline and TMP are synthesized as Ni(II), Cu(II), Co(II), Zn(II), Cd(II), and Hg(II). The complexes were distinguished by solubility, melting point, measurement of conductivity, and the proportion of the metal in flame complexes. Spectroscopic process FTIR and UV-vis. Magnetic susceptibility. Ligand metal complexes were tested in contradiction of four bacteria gram-positive and gram-negative *Escherichia coli, P. aeruginosa, S. aureus,* and *Bacillus* for their antimicrobial activity.[22]

Mixed antibiotic compounds of L-Alanine and TMP were synthesized as Ni(II), Co(II), Cu(II), Hg(II), Zn(II) in addition to Cd(II). The complexes were defined by the application, the measurement of the conductivity, and the calculation of metal percentage in the flame (AAS) complexes, magnetic sensitivity,

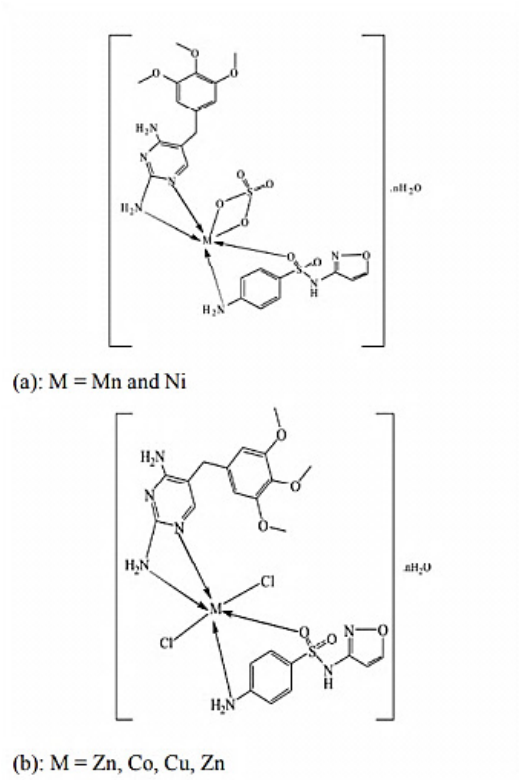
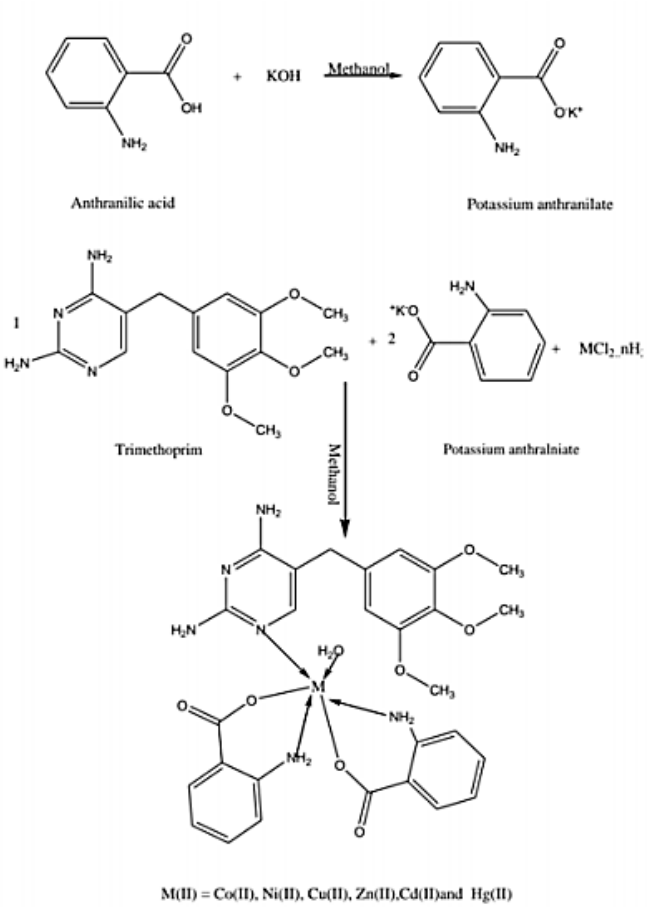
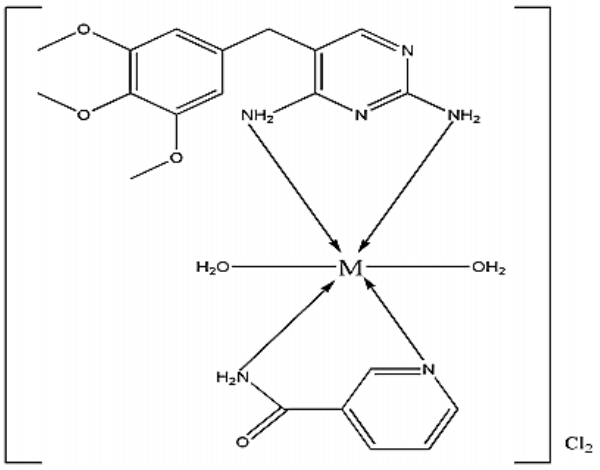



**Figure 2:** Suggested structures of several Metal (II) complexes




**Scheme 1:** Preparing the complexes $[M(Anth)_2(TMP)]$




[M = Mn(II), Cu(II), Fe(II), Zn(II), Co(II)]

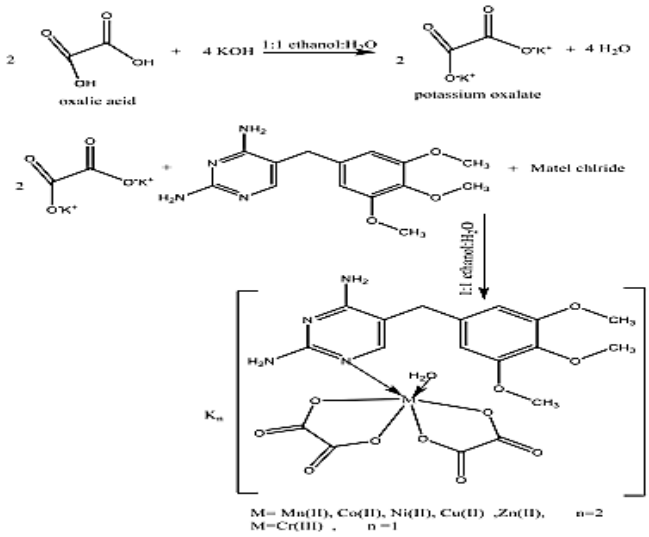
**Figure 3:** Proposed Structure of $[M(NIC)(TMP)(H_2O)_2].Cl_2$

FTIR, and UV-vis. The findings suggest that the bicarbonate ligand was a metal ion (Ala) coordinated by oxygen of a carboxylic group and amine group nitrogen, while a monodentate ligand antibiotic TMP was coordinated with the metal ions by the pyrimidine group nitrogen.[23-25]

In the synthesis of nicotinamide and TMP mixed-line complexes, a variety of transition metal ions have been used. The preparations were based on physical and spectroscopic analytical methods, such as melting-point determination, conductivity measuring, elemental analysis of CHN, and infrared spectroscopy. The findings showed that the ligands were bidental coordinated with the central metal ions. The antimicrobial effects of *S. aureus, P. aureginosa, Klebsiella spp., Escherichia coli,* and *Candida spp.* have been obtained from the complexes. In comparison with ligands, comparative improvement was seen in the synthesized complexes.[24]

Oxalic Acid as prime ligand and TMP as subordinate ligand with formulas K2[M(Oxalate)$_2$(TMP)($H_2O$), as secondary ligand] is identified as new Cr(III), Mn(II), C(II), Ni(II),Cu(II), Zn(II) mixed ligand complexes. FT-IR and UV electronic spectroscopies and magnetic moment, molar conductivity measurements are used to validate the structuring of such complexes. Interestingly, both compounds were tested by calculating the zone of inhibition for the antimicrobial trials of *S. aureus, Bacillus subtilis*, and *Enterobacter Cloacae*.[25]

Based on co-ligand TMP(L2) and Vanadium(V), cadmium (Cd), and silver (Ag) ions in alcohol, a sequence of new metal complexes have been prepared with 4-amino-N-(5-methylisoxazole)-benzene-sulfonamide (L1) as chelating ligand. In solid conditions, the complexes were characterized by flame absorption, simple analyzes CHNS, CFTR, UV-Vis Spectroscopy, conductivity, and magnetic measurements of sensitivity. For CdL1L2, AgL1L2 complexes, tetrahedral geometry was proposed, whereas VL1L2 is the square




**Scheme 2:** The Synthesis Rout of Mixed Ligand Complexes

pyramidal complex. The L1, with the metal ions, has been obviously bident in sulfonyl amide atoms O and N, while in all the complexes, L2 was bident ligand via N and N atoms. Biological activities were investigated in *S. aureus*, *P. aeruginosa,* and *E. coli* in V(IV), Cd(II), Ag(I), TMP, in addition to SMX. The complexes with chelating ligand and co-ligand were evaluated.[26]

The analytical and spectroscopic techniques were used in dual metal complexes, Co(II) and Cd(II), with TMP. It is a 4-coordinate complex of two TMP and two chloride ions. For their structure, TMP acts as a monodentate ligand, a distorted tetrahedral geometry is suggested. The pyrimidine N of the ligand binds a metal. The complexes are tested for Plasmo activity. The consequences indicate that they are less active as compared with the parent ligand. The toxicological research has shown the influence of complex administration in the alkaline kidney, serum and liver function of albino rats, and they have been non-toxic.[27]

Leishmaniasis has been a parasite condition caused by Leishmania protozoa, a genus with very limited options for treating and affecting vulnerable undeveloped populations. Many complications, like high toxicity, high cost, and parasite resistance, are presently present, and new therapeutic agents are required urgently. In this respect, new complexes have synthesized, characterized and given in vitro the leishmanicidal potential [RuCl3(TMP)(dppb)], [PtCl(TMP)(PPh3)2]PF6 as well as [Cu(CH3COO)2(TMP)2], PPH3=tripfenylphosphine are evaluated in (dppb=1,4-bis(diphenylphosphino)butanes). Infrarot, UV, cyclic voltammetry, measurement of molar conductance, elemental analysis, and NMR experiments characterized the complexes. Excellent, it has been shown that [PtCl(TMP)(PPh3)2]PF6 complex is a promising applicant for a new therapeutic leishmanicidal in combination with low toxicity.[28]

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