

Synthesis, Characterization and Antimicrobial Studies of Salicylic Acid Complexes of Some Transition Metals

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ABSTRACT: Salicylic acid complexes of Mn^{2+} , Fe^{2+} , Co^{2+} , Ni^{2+} , and Cr^{3+} , Mn^{3+} , Fe^{3+} , Co^{3+} metal ions were synthesized in ethanol solution. It was observed that the divalent ions gave better yield than the trivalent ones. The complexes were characterized on the basis of the following properties: solubility, electrical conductivity, FTIR and UV-visible spectrophotometry to determine the mode of binding of the ligand to each of the metal ions. The complexes were found to be slightly soluble in distilled water, but soluble in polar organic solvents, an indication that they are molecular compounds. However, their low conductivity values signify non-electrolytic nature of the compounds. The shifting of the band at 1689.70 cm^{-1} to lower values in all the complexes and the vibration centered around 3522.13 cm^{-1} assigned to $\nu(OH)$ indicate that the carboxylic and the hydroxyl groups were involved in coordination to the metal ion, implying that the ligand is bidentate. Inhibition properties of the complexes against three fungi showed that the complexes have higher antimicrobial activity than the ligand which could be attributed to chelation. It appeared that the antifungal activity increased with decrease in ionic size. Their anti-fungi activities were, however, lower than that of a standard antifungal drug, griesifulvin.

Keywords: Salicylic acid, Salicylic acid complexes, Synthesis, Characterization, Antimicrobial studies

1. Introduction

Recent researches have shown significant progress in the utilization of transition metal complexes as drugs for treatment of several human disorders like cancer, lymphomas, infections, inflammation, diabetes and neurological disorders, amongst others [1, 2]. For example, pepto-bismol (bismuth subsalicylate) has been found to be very effective in the control of nausea, heart burn, stomach upset and diarrhea [3] and cisplatin [cis-diammine-dichloroplatinum (II)] for the treatment of tumors [1]. Inorganic metal complexes like platinum (II) porphyrins, titanocenedichloride, ruthenium (III) imidazole, ferrocenes and many organometallic analogues exhibit anti-cancer activity [1,4-6]. Silver (I) sulfadiazine, an anti-bacterial metal complex is effective in the treatment of severe burns. Manganese complexes have been screened against a number of pathogenic fungi and bacteria with most of them showing better sensitivity than the ligands [1, 2, 7]. Iron (III) complexes of quinoline have also proved useful in treatment of malaria [1,8]. Transition metal complexes have also been used as anti-inflammatory and anti-arthritis agents, examples like sodium aurothiomalate, aurothioglucose and aurothiopropanol are all gold complexes. Complexes of copper and iron are capable of catalyzing dismutation of the superoxide anion [1]. Manganese (II) complex of biscyclohexylpyridine substituted macrocyclic ligand has been used to treat cell and tissue oxidative injuries by acting as superoxide anion scavenger [1, 9]. Vanadium and chromium complexes significantly relieve glycaemia among patients with diabetes [10].

In this work we report the synthesis, characterization and antimicrobial activity of salicylic acid complexes of some transition metals, viz: Mn^{2+} , Mn^{3+} , Fe^{2+} , Fe^{3+} , Co^{2+} , Co^{3+} , Ni^{2+} and Cr^{3+} ions. This is in furtherance of the sustained interest in the utilization of the transition metal complexes in the treatment of human ailments, against the backdrop of the alarming problems of multi-drug resistant microorganisms, world over.

2. Experimental

2.1 Materials and methods

The salicylic acid complexes of the following transition metal salts were prepared using the method reported elsewhere [11, 12]: Chromium (III) chloride, $CrCl_3 \cdot 6H_2O$; Manganese (II) chloride, $MnCl_2$; Manganese (III) chloride, $MnCl_3$; Iron (III) chloride, $FeCl_3 \cdot 6H_2O$; Cobalt (III) chloride, $CoCl_3 \cdot 6H_2O$; Iron (II) sulphate, $FeSO_4 \cdot 7H_2O$; Cobalt (II) chloride, $CoCl_2 \cdot 6H_2O$; Nickel (II) chloride, $NiCl_2 \cdot 4H_2O$. The melting points of the complexes were determined using Electro-thermal IA 92000 digital melting point apparatus, while solubility was determined in the following solvents: methanol, ethanol and distilled water. The complexes were further

characterized using the Shimadzu FTIR-8400S Infrared Spectrophotometer, Jenway-6305 UV-Visible Spectrophotometer and WTW Conductometer. Thereafter, their antifungal activities were tested against a standard antifungal drug, griesifulvin.

2.2 Preparation of the complexes

2.2.1 Preparation of M^{2+} salicylate complexes

2.760 g of the salicylic acid was dissolved in 20 mL of ethanol. The resulting solution was added to 1.259 g of manganese (II) chloride in 20 mL distilled water and then refluxed for 2 hours. The precipitate formed was filtered off, washed with ethanol and dried in a desiccator over anhydrous calcium chloride for one week. The same procedure was repeated using 2.779 g of iron (II) sulphate, 2.379 g of cobalt (II) chloride and 2.016 g of nickel (II) chloride [13, 14-15].

2.2.2 Preparation of M^{3+} salicylate complexes

3.036 g of the salicylic acid was dissolved in 20 mL of ethanol. The resulting solution was added to 2.665 g of chromium (III) chloride in 20 mL distilled water and refluxed for 2 hours. The precipitate formed was filtered off, washed with ethanol and dried in a desiccator over anhydrous calcium chloride for one week. The same was repeated using 1.614 g of manganese (III) chloride, 2.704g of iron (III) chloride, and 2.734 g of cobalt (III) chloride [13, 15-17].

3. Results and Discussion

Table 1 shows the physical characteristics of the ligand and the metal complexes.

Table 1.Characteristics of the ligand and metal complexes

Sample	Product yield (%)	Colour	M.P (°C)	Physical Appearance	Conductivity μ S/cm	λ_{max} (nm)	IR bands $\nu(C=O)cm^{-1}$
Salicylic acid	-	White	157-159	Powdery	-	340	1689.70
[Cr(sal) ₃]	42.64	Green-white	217-219	Crystalline	91.3	345	1668.48
[Mn(sal) ₂]	60.27	White	220-222	Crystalline	44.5	335	1666.55
[Mn(sal) ₃]	59.23	White	224-226	Crystalline	71.9	335	1669.45
[Fe(sal) ₂]	68.85	Reddish-brown	186-189	Crystalline	13.6	340	-
[Fe(sal) ₃]	55.89	Brown	189-190	Crystalline	121.0	335, 555	1666.55
[Co(sal) ₂]	53.19	Pinkish-Blue	208-210	Crystalline	59.2	335	1677.16
[Co(sal) ₃]	72.36	Pink	13-215	Crystalline	36.5	335	1675.23
[Ni(sal) ₂]	72.36	Light-yellow	220-223	Crystalline	187.4	330	1668.48

- M. P is melting point

The absorption bands below were observed from the spectra of the acid and its complexes (Figures 1 to 9)

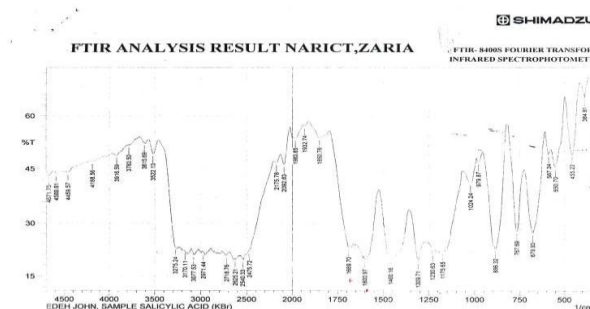
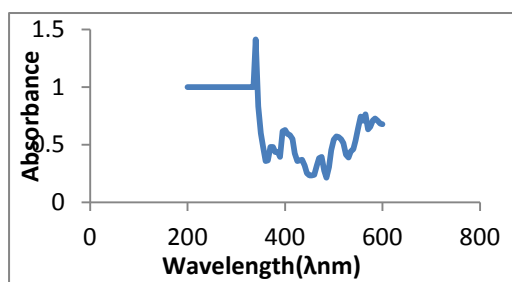


Fig. 1a UV spectrum for salicylic acid

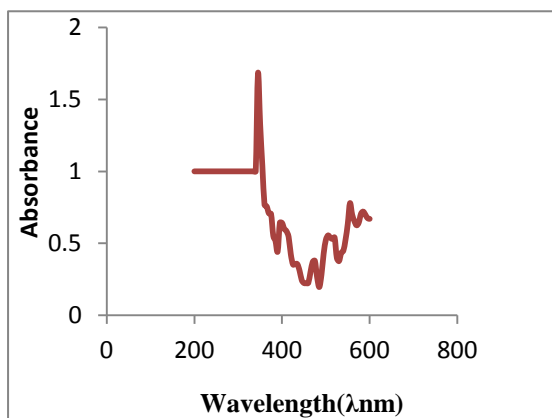


Fig. 1b FTIR spectrum for salicylic acid

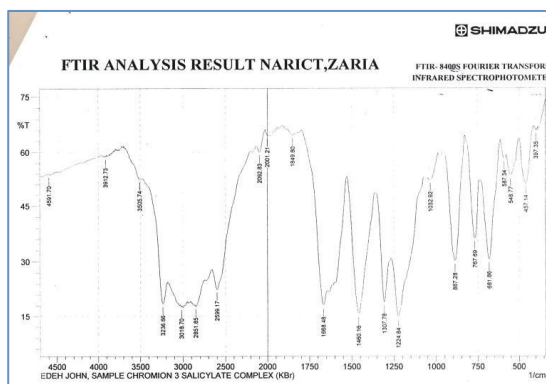


Fig. 2a UV spectrum for chromium (III) salicylate

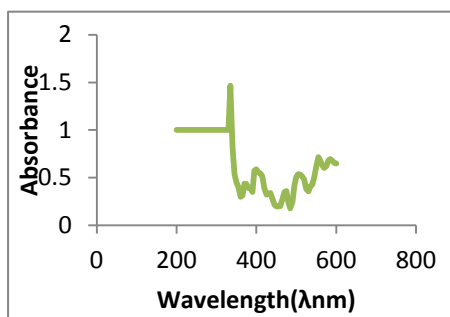


Fig. 2b FTIR spectrum for chromium (III) salicylate complex

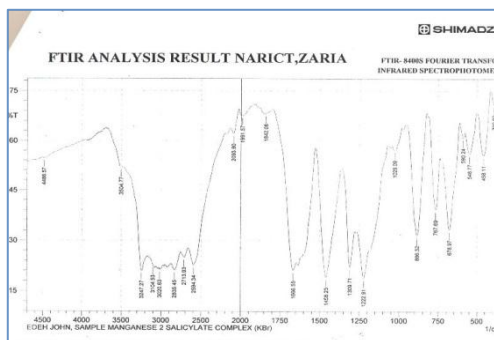


Fig. 3a UV Spectrum for manganese (II) salicylate

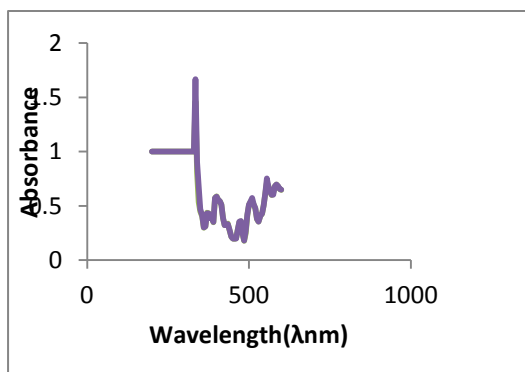


Fig. 3b FTIR Spectrum for manganese (II) salicylate complex

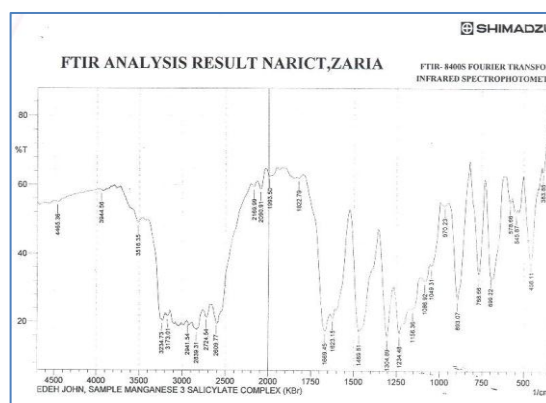


Fig. 4a UV Spectrum for manganese (III) salicylate

Fig. 4b FTIR Spectrum for manganese (III) salicylate complex

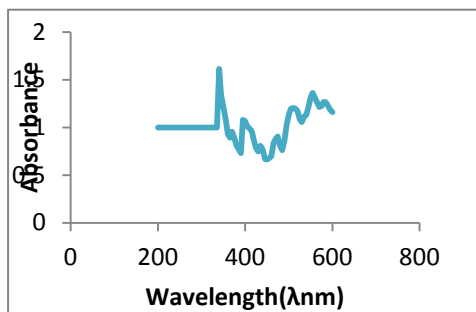


Fig 5a UV spectrum for iron (II) salicylate

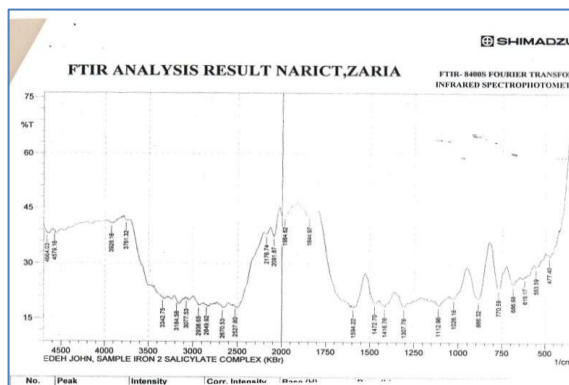


Fig 5b FTIR spectrum for iron (II) salicylate

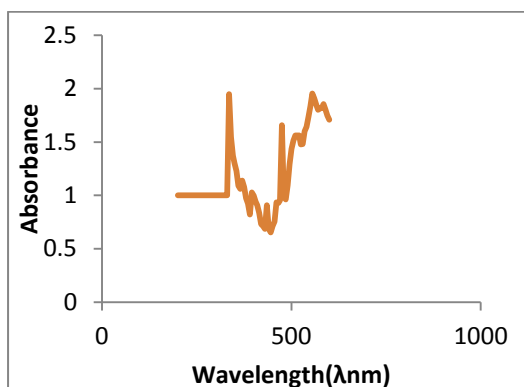


Fig. 6a UV spectrum for iron (III) salicylate

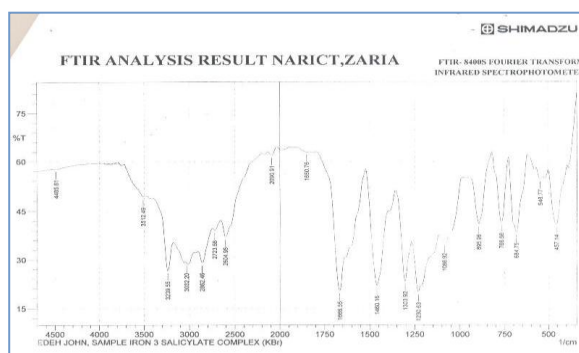


Fig. 6b FTIR spectrum for iron (III) salicylate complex

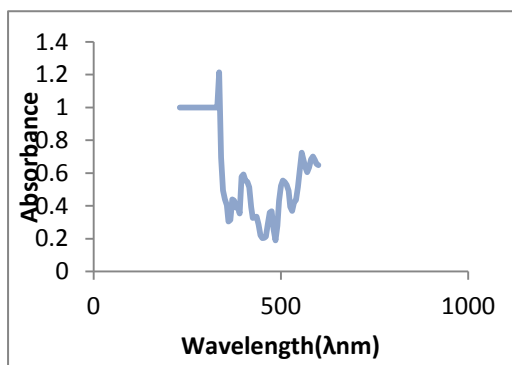


Fig. 7a UV spectrum for cobalt (II) salicylate

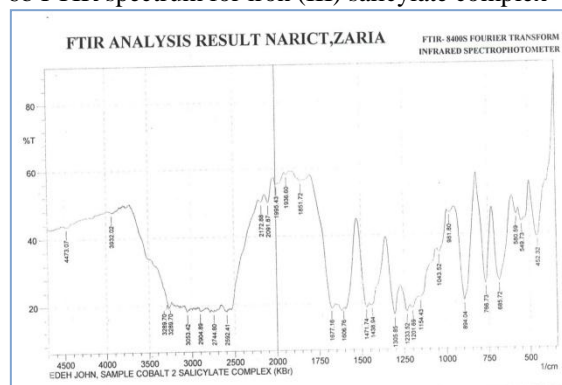


Fig. 7b UV spectrum for cobalt (II) salicylate complex

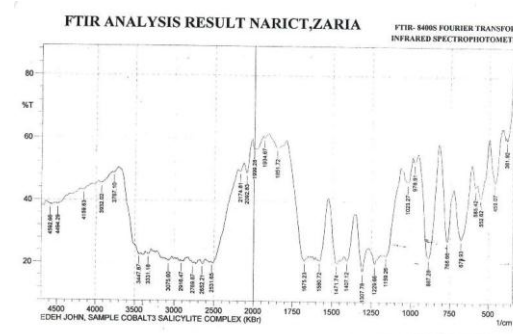
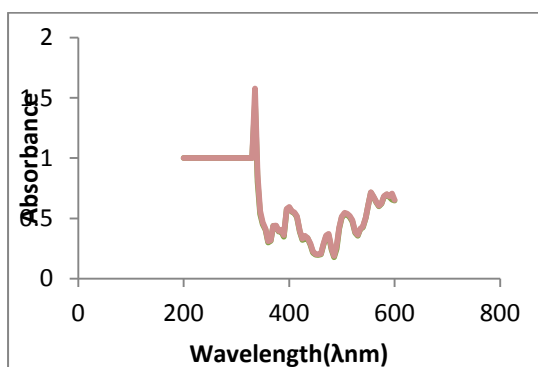


Fig. 8a UV spectrum for cobalt (III) salicylate

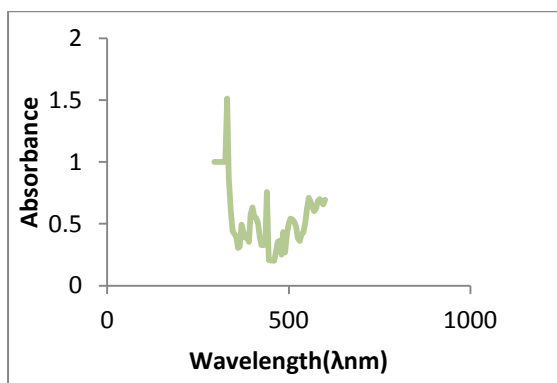


Fig. 8b FTIR spectrum for cobalt (III) salicylate

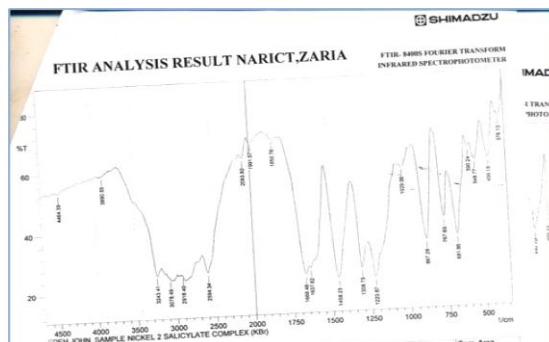


Fig. 9a UV spectrum for nickel (II) salicylate

Fig. 9 FTIR spectrum for nickel (II) salicylate

Table 2. Solubility of the ligand and metal complexes in different solvents and their conductivities in acetone

Ligand/ Complex	Distilled water	Ethanol	Methanol	Conductivity $\mu\text{S}/\text{cm}$
Salicylic acid	NS	S	S	-
[Cr (sal) ₃]	SS	S	S	91.30
[Mn(sal) ₂]	SS	S	S	44.50
[Mn(sal) ₃]	SS	S	S	71.9
[Fe(sal) ₂]	SS	S	S	13.60
[Fe(sal) ₃]	SS	S	S	121.0
[Co(sal) ₂]	SS	S	S	59.20
[Co(sal) ₃]	SS	S	S	36.50
[Ni(sal) ₂]	SS	S	S	187.4

The reduction in the frequency of $\nu(\text{C}=\text{O})$ vibrational band were expected outcomes if the complexes were generated. The assignment and interpretation of vibrations below 1500 cm^{-1} are difficult to make with certainty because they occur in the finger print region where coupled vibrations occur. Metal-ligand vibrations are mostly observed below 800 cm^{-1} [18, 19].

Based on the data generated from ultra violet and infrared spectrophotometric analyses the following structures (fig.1 and 2 below) were proposed.

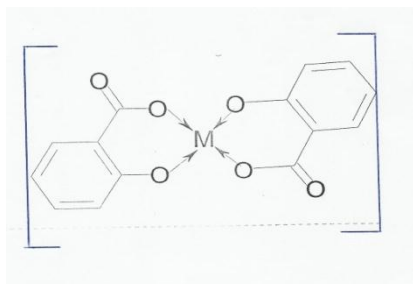


Fig. 1 Structure of M^{2+} salicylate complex

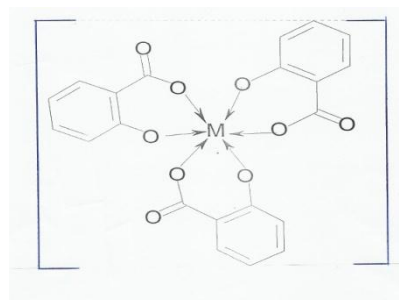
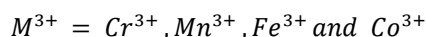
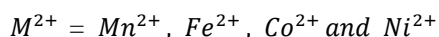


Fig. 2 Structure of M^{3+} salicylate complex



The above structures were proposed based on the conditions of the following reactions:



The antifungal activity of the metal salicylate complexes against the fungi at concentration of 100 mg/mL is given in Table 3. All the synthesized complexes showed comparative good activity against the fungi. The activity, however, follows the order: $Co^{2+} > Co^{3+} > Fe^{3+} > Fe^{2+} > Ni^{2+} > Mn^{2+} > Mn^{3+} > Cr^{3+}$ for *Aspergillus niger* of which M^{2+} showed the order $Co^{2+} > Fe^{2+} > Mn^{2+} > Ni^{2+}$ and M^{3+} showed the trend $Co^{3+} > Fe^{3+} > Mn^{3+} > Cr^{3+}$. *Aspergillus hereus* had the trend: $Co^{2+} > Co^{3+} > Ni^{2+} > Fe^{3+} > Fe^{2+} > Mn^{3+} > Cr^{3+} > Mn^{2+}$ with M^{2+} of the complexes showing $Co^{2+} > Ni^{2+} > Fe^{2+} > Mn^{2+}$ while M^{3+} showed $Co^{3+} > Fe^{3+} > Mn^{3+} > Cr^{3+}$. For *Tychophyton mantagrophytes* the order was observed as $is Co^{2+} > Co^{3+} > Ni^{2+} > Fe^{3+} > Fe^{2+} > Cr^{3+} > Mn^{2+} > Mn^{3+}$, of which M^{2+} followed $Co^{2+} > Ni^{2+} > Fe^{2+} > Mn^{2+}$ and M^{3+} showed the trend $Co^{3+} > Fe^{3+} > Cr^{3+} > Mn^{3+}$. In general, it was observed that antifungal activity increased with decrease in ionic size.

Table 3. Antifungal activity of griesifulvin. , salicylic acid and the synthesized metal complexes

S/N	Complex	<i>Aspergillus niger</i> (cm)	%	<i>Aspergillus hereus</i> (cm)	%	<i>Trychophyton mantagrophytes</i> (cm)	%
1	Griseofulvin	5.00	100	5.00	100	5.00	100
2	Salicylic acid	3.05	61	3.00	60	2.50	50
3	[Cr(sal) ₃]	3.10	62	3.00	60	2.60	52
4	[Mn(sal) ₂]	3.25	65	2.90	58	2.55	51
5	[Mn(sal) ₃]	3.25	65	3.00	60	2.50	50
6	[Fe(sal) ₂]	3.45	69	3.35	67	3.00	50
7	[Fe(sal) ₃]	3.50	70	3.40	68	3.05	60
8	[Co(sal) ₂]	3.55	71	3.60	72	3.30	61
9	[Co(sal) ₃]	3.50	70	3.55	71	3.30	66
10	[Ni(sal) ₂]	3.40	68	3.45	69	3.20	64

The preliminary investigation of antimicrobial activities of the metal complexes in Table 3 revealed that the inhibitory ability of the metal complexes is notably higher than the ligand, though less than the compared standard antifungal drug, griesifulvin. And the actions against *Aspergillus niger* and *Aspergillus hereus* are comparatively same but greater than that of *Trychophyton mantagrophytes*.

In all, the cobalt complexes showed the highest activity. However, whether this effect was due to the complex or the cobalt atom was not investigated. Furthermore, antimicrobial activity of the metal chelates can be explained on the basis of chelation theory which may enhance the biochemical potential of a bioactive species. This is because on chelation, the polarity of the metal ion will be reduced due to the overlap of the ligand orbital and partial sharing of the positive charge of the metal ion with donor groups and possibly π -electron delocalization over the whole molecule [19-21]. This may enhance the penetration of the complex into the lipid membranes enabling it to block the metal binding sites in the enzymes of micro-organisms. These

complexes also disturb the respiratory processes of the cell and thus inhibit protein synthesis which restricts further growth of the organism.

4. Conclusion

Selected metal complexes of M^{2+} and M^{3+} were synthesized using salicylic acid and their antifungal activities were assessed. It was found that the complexes had antifungal activities against *Aspergillus niger*, *Aspergillus hereus*, and *Trychophyton mantagrophyte*. This justified the use of transition metal complexes as therapeutic agents and as potential antibiotics.

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