Synthesis and Antitubercular Activities of Cu(II) Metal Complexes with some Semicarbazide Derivatives.

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ABSTRACT

The emergence of new cases, the increased incidence of multi-drug resistant strains of *Mycobacterium tuberculosis*, and the adverse effects of first- and second-line antituberculosis drugs has led to renewed research interest in metal drug complexes in the hope of discovering new Antitubercular drugs.

Three semicarbazide derivatives were synthesized, starting from the condensation reaction of semicarbazide with potassium thiocynate to obtain bithiourea (BTU). 2, 5-diamino-1,3,4-thiadiazole(DT) was obtained by cyclisation of bithiourea using 3% hydrogen peroxide as catalyst. Benzoyl semicarbazone (BSC) a Schiff base product was obtained through Mannich reaction (condensation). The metal complexes of BTU, DT and BSC were prepared and the complexes were formulated as $Cu(BTU)_2$, $Cu(DT)_2$ and $Cu(BSC)_2$. The complexes were characterized by elemental analysis, conductivity, Infrared, Ultraviolet/visible and magnetic moment. In all cases copper (II) coordinated with the three ligands and the suggested structures were tetrahedral or distorted octahedral complexes.

The complexes showed activities against *mycobacterium tuberculosis strain $H_{37}RV$ in-vitro*. These results preliminary indicated the possible use of the prepared complexes for treatment of tuberculosis infections in order to overcome the resistance developed with most basic drugs used in tuberculosis chemotherapy.

(Keywords: semicarbazide derivatives, condensation, cyclisation, antimicrobial, Antitubercular, characterized)

INTRODUCTION

Metal coordination to biologically active molecules can be used as a strategy to enhance their activity and overcome resistance. For instance, metal complexes of thiosemicarbazones can be more active than the free ligand, or they can be employed as a vehicle for activation of the ligand as the cytotoxic agent (West *et al.*, 1993; Beraldo and Gambino, 2004; Mendes *et al*., 2007).

Aminourea based derivatives exhibit a range of bioactivities, including anti-angiogenic, anti-tumor, anti-malarial, anti-inflammatory and analgesic, anti-tubercular, anti-glaucoma, anti-HIV, cytotoxic and antimicrobial properties (Obaleye *et al.,* 2011).

The Antitubercular activities possessed by semicarbazide and thiosemicarbazide derivatives prompted us to synthesize some compound from semicarbazide and complex them with metals to enhance their activities and test against *mycobacterium tuberculosis.*

Tuberculosis (TB), a member of the *Mycobacterium tuberculosis* complex (MAC), causes three million deaths a year worldwide (Raviglione *et al*., 1995). The disease is associated with impoverished economic conditions. The resurgence of *M. tuberculosis* infection in the developing countries is due to immigration, the emergence of drug-resistant

strains, inadequate treatment, continuing poverty, malnutrition, overcrowding, alcoholism and the AIDS epidemic (Prescott et al., 2005).

Following the discovery of isoniazid, there have been no new classes of Antitubercular drugs in the past 40 years (Whalen *et al*., 1995). Moreover, there has been a recent and disturbing increase in the number of tubercular cases that are caused by organisms which are resistant to the first-line drugs such as isoniazid, rifampicin, ethambutol, streptomycin, and pyrazinamide (Sriram *et al*., 2005).

Infectious microbial disease causes worldwide problem, because microbes have resisted prophylaxis or therapy longer than any other form of life. In recent decades, problems of multidrug-resistant microorganisms have reached an alarming level in many countries around the world. Resistance of anti-microbial agents such as β-lactam antibiotics, macrolides, quinolones and vancomycin by different species of bacteria has caused increased important global problems (Shingalapur et al., 2009).

Semicarbazide and its derivatives are reported to be physiologically and pharmacologically active and find applications in the treatment of several diseases. Considering these we thought it worthwhile to incorporate metal ion ring into various derivatives synthesized to have synergistic effect.

EXPERIMENTAL

Materials and Methods

All reagents and solvents used were reagent grade and were used without prior purification unless otherwise stated.

Elemental analyses were performed at the Pontificia Universidade Catolica, Rio de Janeiro, Brazil. Molar conductivity measurements were performed in DMF 10^{-3}mol/L using Genway 4200 conductivity meter.. The IR spectra were acquired using SP3-30 Perkin-Elmer FT-IR spectrometer and in the wave number region 4000 – 400 cm^{-1}.

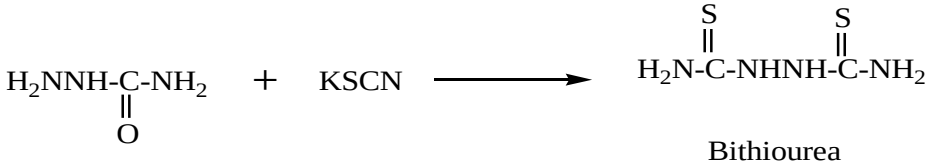
The spectra were recorded as KBr disks. ^{1}H NMR (300 MHz), and ^{13}C NMR (75 MHz) spectra were recorded on Bruker spectrometer and were obtained by dissolving the complexes in $DMSOd_6$. The chemical shifts were expressed as δ (ppm) from internal reference standard TMS (^{1}H NMR).

The molar magnetic susceptibilities of the powdered samples were measured using Faraday Balance Model 7650 using $Hg[Co(SCN)_4]$ calibrant. The ultraviolet/visible analysis was carried out on Genesys.10S V1.200 spectrophotometer. Thin layer chromatography was carried out using TLC plate coated with silica gel.

SYNTHESIS OF THE LIGANDS

Preparation of Bithiourea

25.4g (0.22mole) semicarbazide Hydrochloride and 21.4g (0.22mole) potassium thiocyanate were introduced into a round-bottomed flask. The mixture was dissolved in 60ml water, refluxed for 3 hours and the solution was allowed to cool. White crystals separated out and the separated crystals were filtered out and dried at $100^{O}C$ in the oven for 2hours. The product was thereafter recrystallized from boiling water.



Equation of the reaction

Properties:

Percentage yield of Bithiourea = 95.12%.

Melting point: 207 – 208^{O}C.

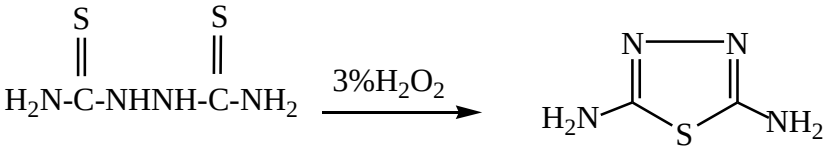
Color: White.

Appearance: Crystalline Powder.

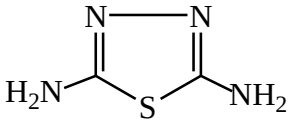
Solubility: Found soluble in (a) hot water (b) Aqueous ethanol, DMSO and DMF.

Preparation of the 2, 5-Diamino-1,3,4-Thiadiazole (L)

30g (0.2mol) of bithiourea was introduced into a 250 cm^3 round bottomed flask and 40 cm^3 of 3% H_2O_2 was added. The mixture was refluxed at 50 - 60°C for 1 hr with continuous stirring. The product was then filtered under vacuum and dried at 100°C in the oven and the percentage crude yield was determined. It was thereafter recrystallized from boiling water



Bithiourea



2,5-diamino-1,3,4-thiadiazole

Equation of the reaction

The cyclisation of bithiourea were performed by 3% hydrogen peroxide, H_2O_2, the probable mechanisms of this cyclisation is shown in Scheme 1.

Properties:

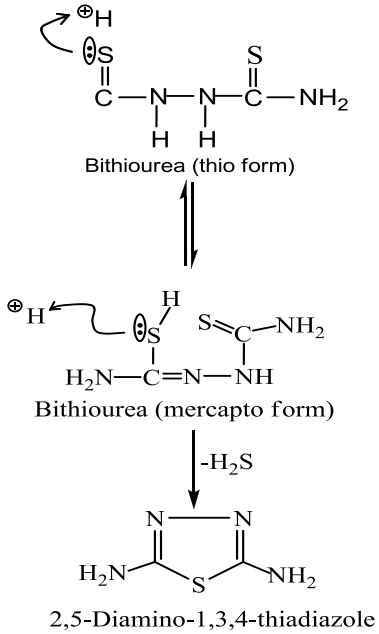
Percentage Yield: 96.42%

Melting point: 202 -203^{O}C

Color: White

Appearance: Amorphous Powder

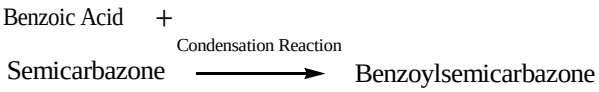
Solubility: Soluble in hot water, N,N-dimethylformamide and aqueous ethanol.



Scheme 1

Synthesis of Benzoylsemicarbazone
(Leovac *et al*., 2004**)**

Benzoyl semicarbazone was obtained in good yield by the condensation reaction of aqueous or alcoholic solution of benzoic acid and the corresponding semicarbazone salt. This was carried out by adding 13.42g (0.11Mole) of benzoic acid and 25.42g (0.11mole) of semicarbazone together in 40ml ethanol. The mixture was heated for 30minutes on a water bath until a crystalline shiny powder was obtained. It was then filtered and dried in a desiccator at room temperature.



Equation for the reaction

Properties:

Percentage yield: 85.26%

Melting point: 65^{O}C

Color: White

Appearance: Crystalline shiny powder

Solubility: Found soluble in (a) water (b) aqueous ethanol (c) Acetone.

Synthesis of Copper (II) Metal Complexes

All complexes were obtained by the simple template method, i.e. by the reaction of ready-made ligands, and metal salts, mainly in warm alcoholic (less often aqueous) solution under the normal laboratory condition. An aqueous or ethanolic solution of the metal salt was mixed with an aqueous ethanolic solution of Bithiourea, 2,5-diamino-1,3,4-thiadiazole and Benzolysemicarbazone (which was dissolved in minimum amount of the solvent) (i.e., 0.02 mole of Ligands and 0.01 mole of the metal salt). The reaction mixture was heated in a 250ml round bottomed flask for 15 minutes on a water bath until there was change of coloration, indicating the precipitates of the complexes. The reaction mixture was then reduced to about one third after the metal complex separated out on cooling. The complex formed was recovered from the solution by filtration. It was washed and recrystallized from ethanol and then dried in a desiccator over $CaCl_2$.

Yields: $Cu(BTU)_2$= 95.12%, $Cu(DT)_2$ = 87.3% and $Cu(BSC)_2$= 85.2%

$Cu(BTU)_2$: Light green solid. IR: (KBr, cm^{-1}); 3431.10b, 2164.00w, 1631.66s, 1550.87w, 1474.12w, 1084.17b, 605.00w, 410.53str. Uv/Visible: 208nm (48077cm^{-1}), 274nm (36496cm^{-1}), 493nm (20284cm^{-1}), 538nm (18587cm^{-1}). Anal. Calc. For $CuC_4H_{12}N_8S_4$: C, 13.22; H, 3.30; N, 30.81; S, 32.21; Cu, 17.47. Found: C, 13.19; H, 3.32; N, 30.72; S, 32.11; Cu, 17.81.

$Cu(DT)_2$: Dark green solid. IR: (KBr, cm^{-1}): 3424.82b, 1631.15s, 1407.37s, 1222.68s, 1057.20str, 762.98str, 593.97str Uv/Visible: 229nm (43668cm^{-1}), 277nm (36101cm^{-1}), 361nm (27700cm^{-1}), 364nm (27473cm^{-1}). Anal. Calc. For $CuC_4H_8N_8S_2$: C, 16.24; H, 2.71; N, 37.90; S, 21.66; Cu, 21.49. Found: C, 16.22; H, 2.73; N, 37.89; S, 21.65; Cu,21.51.

$Cu(BSC)_2$: Light green solid. IR: (KBr, cm^{-1}): 3400.02b, 1638.08vs, 1395.40s, 1027.39s, 935.55w, 707.66str, 571.73s. Uv/Visible: 202nm(49505cm^{-1}), 238nm(42017cm^{-1}), 313nm(31949cm^{-1}), 457nm(21882cm^{-1}). Anal. Calc. For $CuC_{18}H_{16}N_6O_4$: C, 53.53; H, 3.97; N, 20.82; O, 5.95; Cu, 15.74. Found: C, 53.52; H, 3.95; N, 20.80; O, 5.93; Cu, 15.72.

***IN-VITRO* ANTITUBERCULAR TEST**

Determination of minimal inhibitory concentration

The activity of the complexes against M. tuberculosis virulent strain H_{37}Rv was determined *in vitro* as described below:

Antitubercular activity was evaluated against *Mycobacterium tuberculosis* H_{37} Rv using Microplate alamar blue assay (MABA) method (Collins *et al*, 1997; Enayat and Ashraf, 2004). Antitubercular susceptibility test was performed in black, clear-bottomed, 96-well microplates (Packard Instrument Company, Meriden, Conn., USA) in order to minimize background fluorescence. Initial drug dilutions were prepared in dimethylsulfoxide and subsequent two-fold

dilutions were performed in 0.1 ml of 7H9GC media in the microplates. An aliquot (100 µl) of 2000CFU/ml of *M. tuberculosis* H_{37} Rv were added to each well of 96-well microtitre plate containing test compounds. Three control well plates containing drug and medium, bacteria and medium, and medium only were also prepared. All microtitre plates were incubated at 37 °C for seven days. At day 7 of incubation, Alamar Blue dye solution (20 µl Alamar Blue solution and 12.5 ml of 20% Tween 80) was added to all the wells and the plates re-incubated at 37 °C for 24 h.

Fluorescence was measured in a Victor II multilabel fluorometer (Perkin Elmer Life Sciences Inc., Boston, MA, USA) and MIC was determined. The minimum inhibitory concentration (MIC), concentration that inhibits the colony forming ability of M. tuberculosis was determined by incorporating decreasing concentrations of the test compounds dissolved in dimethylsulfoxide in Middlebrook 7H9GC agar medium. MIC values represent mean of three separate experiments.

RESULTS AND DISCUSSION

The complexes $[Cu(L)_2]$ where L = Bithiourea (BTU), 2,5-diamino-1,3,4- thiadiazole (DT), and Benzoylsemicarbazone (BSC) were obtained by reaction between the respective ligand and the copper(II) salt $CuCl_2.4H_2O$ in aqueous medium. The desired product is immediately formed as a precipitate upon addition of the ligand to the copper salt.

The elemental analyses were in good agreement with the proposed formula for the three compounds. It was observed that the copper (II) complexes with various ligands were formed after few minutes, except that of $Cu(DT)_2$ which occurs more slowly. The coordination sites were found to be nitrogen, sulphur and oxygen sequenced towards the metal ion, as discussed within this paper and in previous work (Obaleye *et al.,* 2011. Adediji *et al.,* 2011).

In the majority of the complexes described in the literature, the ligands coordinated in a tridentate manner via the nitrogen of the hydrazine, nitrogen of the amine, the sulphur atoms and deprotonated oxygen atom in the cyclic compound, where the metallic ion forms a stable six-membered ring chelate.

In the IR spectra of these complexes it is possible to observe the disappearance or a high shifts of the absorption bands in various region due to formation of bonds between the metallic ion and the ligands.

The Cu (II)-BTU shows a magnetic moment value of 1.90 B.M. which is larger than spin only value 1.73B.M. This is not common in mononuclear Copper (II) complex due to the mixing of some angular moment from the closely lying excited state via spin-orbit coupling. This support its distorted octahedral stereochemistry (Mane *et al,* 2001). The Cu (II)-DT magnetic moment value is 2.30 B.M.

The Cu (II)-BSC complex shows a μ_{eff} value of 2.00B.M which corresponds with a high spin octahedral geometry (Mane et al., 2001). A d^9 ion in an octahedral environment has an E ground state term with higher T term of the same multiplicity. Spin-orbit coupling causes a mixing of orbital contribution from the T term into the ground term. Depending on the magnitude of orbital contribution, a moment of 1.73-2.5 B.M. is expected (Mane *et al.,* 2001. Patel and Faniran, 1977).

IR for Bithiourea

The IR spectrum of the ligand exhibited a very strong broad bands with a peak maximum at $3400cm^{-1}$- $3100cm^{-1}$, which are ascribed to the υ(OH) vibration of hydroxymethyl group and H_2O along with υ(NH_2) and υ(NH) vibrations (Blicchi *et al.,* 2002).

The decrease and shifts in the absorption frequency of the υ(NH) band for the complexes relative to free ligand is a strong evidence of coordination with one of the N-H bands of Bithiourea.

The very strong υ(C=S) band in Bithiourea at $1430cm^{-1}$. This is close to the value characteristic for the majority of the ligand, in the complexes shifted to higher energies by 10-$20cm^{-1}$. A number of bands in the range 1640-$1400cm^{-1}$ in the spectra of both ligands and complexes are ascribed to υ(C=N) and δ(NH_2) of the chain.

IR for 2,5-DT

The spectra of 2,5-Diamino-1,3,4-Thiadiazole was compared with the spectra of its complexes.

The absorption band at a high energy of 3195 cm^{-1} in the spectrum of the ligand is attributed to υ(NH) and υ(NH^{+}) of the hydrazine. The bands have been shifted in the spectra of the complexes. The shifting indicates evidence of coordination. Strong absorption at 1536cm^{-1} in the free ligand has undergone hypsochromic shifts in the metal complexes. Bands at 1430cm^{-1} is assigned for υ(C-S), while bands at 1295cm^{-1} is assigned for υ(C=N). They have undergone shifts in the metal complexes which indicate the evidence of coordination at those sites respectively. Bands between 800-900cm^{-1} which were absent in the free ligand are assigned to M-L i.e metal to ligand coordination (Bakhtiar and Ochiai.1999)

IR for BSC

It shows band above 3000cm^{-1} which are due to υ(NH_2), υ(NH) and υ(H_2O) vibrations. These bands are normally indistinguishable (Kharitonov and Mach Khoshvili,1971). The band at 3300cm^{-1} in the spectrum of benzoyl Semicarbazone is due to amino group vibrations. The increase in the frequency of this band relative to the position in the free ligand suggests lack of coordination through the primary amino nitrogen (Allan *et al,* 1984). The υ(C=O) band appears at 1688cm^{-1} in the spectra of the ligand. The position of the bands represents a decrease in frequency of 40-60cm^{-1} compared to the free ligand. This indicates coordination through the carbonyl oxygen.

The υ(C=N) and δ(NH_2) bands appears it 1602cm^{-1}. The observed increase indicate no coordination through that point. Low frequency vibrations around 500cm^{-1} are assigned to metal-ligand vibrations.

UV/Visible Spectra of Cu-BTU, Cu-DT and Cu-BSC

In Cu-BTU complex; Copper has an electronic configuration of d^9 and a spectroscopic ground state term symbol of ^2D. ^2D orbital is split in a tetrahedral field or in a distorted octahedral field into sub-energy levels ^2E, ^2T and ^2Eg, $^2T_{2g}$, respectively.

There are two weak absorption bands at 20284cm^{-1} and 18587cm^{-1} which is due to d-d transitions. Complex probably has an octahedral structure though distorted due to inherent Jahn-Teller effect on a d^9 system (Cotton and Wilkinson, 1981).

In Cu-DT complex; Copper has an electronic configuration of d^9 and a spectroscopic ground state term symbol of ^2D. The ^2D orbital is split in a tetrahedral field or in a distorted octahedral field into sub-energy levels ^2E, ^2T and ^2Eg, $^2T_{2g}$, respectively.

There are four absorption bands at 43668cm^{-1}, 36101cm^{-1}, 27700cm^{-1}, and 27473 cm^{-1} which is due to charge transfer transitions. The complex probably has an octahedral structure, though distorted, due to inherent Jahn-Teller effect on a d^9 system (Cotton and Wilkinson, 1981).

In Cu-BSC complex; Copper has an electronic configuration of d^9 and a spectroscopic ground state term symbol of ^2D. The ^2D orbital is split in a tetrahedral field or in a distorted octahedral field into sub-energy levels ^2E, ^2T and ^2Eg, $^2T_{2g}$, respectively.

There is one weak absorption band at 21882 cm^{-1} which is due to d-d transition. The complex probably has an octahedral structure though distorted due to inherent Jahn-Teller effect on a d^9 system (Cotton and Wilkinson, 1981).

The activity of the complexes against mycobacterium tuberculosis virulent strain $H_{37}RV$ was determined. The minimum inhibitory concentration (MIC) against M. tuberculosis was determined and results are presented in Table 1.

All the complexes were active within each series inhibiting bacterial growth at 0.36µg/mL, 0.31µg/mL and 0.32µg/mL.

In general all of the complexes exhibited good activity; all of them were more active than Isoniazid.

It is interesting to note that some of the currently used Antitubercular drugs, such as pyrazinamide, isoniazid and ethionamide, also possess electron withdrawing groups as its pharmacophore (Pablos-Mendez et al., 2002). The presences of electron withdrawing group in the ligands used suggest the reasons for its good Antitubercular activity.

CONCLUSIONS

The ligands reacted with Cu (II) ion furnishing compounds [ML_2]. The ligands coordinated with the copper in the most common manner expected as observed in the literature and previous related work reported. Tentative octahedral structures were proposed for the complexes. The complexes show good Antitubercular activity. The findings of this work should be helpful to medicinal chemists involved in further drug development in this field.

REFERENCES

1. Adediji, J.F, M.A. Adebayo and J.A. Obaleye. 2011. "Synthesis, Toxicological and Antimicrobial Activities of Mn(II) and Fe(III) with N- and S-donor ligand". *Asian Journal of Applied Sciences.* 4(4): 392-402.

2. Allan, J.R, G.M. Balille, and N.D. Baird. 1984. "Some First Row Transition Metal Complexes of Isoniazid". *Journal of Coordination Chemistry*. 13(2):83-88.

3. Beraldo, H. and D. Gambino. 2004. *Mini Rev. Med. Chem*. 4:31–39.

4. Bakhtiar, R. and E.I. Ochiai.1999. "Phamacological Application of Inorganic Complexes". *General Pharmacology*. 32(5):525-540.

5. Blicchi, M., F. Ferrari, E. Bisceglie, G. Leporati, P. Pelosi, and P. Tarasconi. 2002. "Synthesis, Solution Chemistry, X-ray Structure and Biological Activity of Novel Pyridoxal Thiosemicarbazone Derivatives". *Bull. Chem.Soc. Japan.* 75:781.

6. Collins, E.A. and S.G. Franzblow. 1997. "Microplate Alamar Blue Assay Versus BACTEC 460 System for High Throughput Screening of Compounds against *Mycobacterium tuberculosis* and *Mycobacterium avium*". *Antimicrob Agents Chemother*. 41:1004–1009.

7. Cotton, F.A. and G. Wilkinson. 1981. *Advanced Inorganic Chemistry, 4th edition*. John and Sons: New York, N.Y. 628, 641, 811-816.

8. Enayat, I.A. and H.A. Ashraf. 2004. "Synthesis and Antitubercular Activity of 6-chloro (unsubstituted)- 2-methoxy-9-substituted Acridine Derivatives". *Arch Pharm. Res*. 27:713–719.

9. Kharitonov, Y.Y. and R.I. Mach Khoshvili .1971. "Complexes of Platinum (II) with Benzoyl Hydrazine". *Russian Journal of Inorganic Chemistry.* 16(4):604-6.

10. Leovac, V.M, V.S. Jevtovic, L.S. Jovanovic, and G.A. Bogdanovic .2004. "Metal Complexes with Schiff-Base ligand-Pyridoxal and Semicarbazide Based derivatives". *J. Serb. Chem. Soc*. 70(3):393-422.

11. Mane, P.S, S.G. Shirodkar; B.R Arbad, and T.K. Chondhekar. 2001. "An Unsual Dimeric Structure of a Cu(II) bis (thiosemicarbazone) Complex". *Indian J. Chem.* 40A(6): P.648.

12. Mendes, I.C., J.P. Moreira, A.S. Mangrich, S.P. Balena, B.L. Rodrigues, and H. Beraldo. 2007. *Polyhedron*. 26:3263–3270.

13. Obaleye, J.A, J.F. Adediji and M.A. Adebayo. 2011. "Synthesis and Biological Activities on Metal Complexes of 2,5-Diamino-1,3,4-thiadiazole Derived from Semicarbazide Hydrochloride". *Molecules*. 16:5861-5874.

14. Patel, K.S. and J.A. Faniran. 1977. "Magnetic and Spectral Properties of the Manganese(II), Iron(II), Cobalt(II), Nickel(II), Copper(II), Zinc(II), and Palladium(II) Complexes of 1-(3-pyridyl)-1,3 Butanedione and 4,4,4-trifluoro-1-(3-pyridyl-1,3-butanedione". *Journal of Inorganic and Nuclear Chemistry*. 39:1143-7.

15. Pablos-Mendez, A., D.K Gowda, and T.R. Frieden. 2002. "Controlling Multidrug-Resistant Tuberculosis and Access to Expensive Drugs: A Rational Framework". *Bull World Health Organ*. 80:489-495

16. Prescott, L.M., J.P. Harley, D.A. Klein. 2005. "Human Diseases Caused by Viruses". In: *Microbiology 4th ed.* WCB/McGraw Hill: Boston. 743-752.

17. Raviglione, M.C, D.E. Snider, and A. Kochi. 1995. "Global Epidemiology of Tuberculosis. Morbidity and Mortality of a Worldwide Epidemic". *JAMA*. 273:220-226.

18. Shingalapur, R.V., K.M. Hosamani, and R.S. Keri. 2009. *European Journal of Medicinal Chemistry*. 44:4244–4248.

19. Sriram, D., P. Yogeeswari, and K. Madhu. 2005. "Synthesis and in-vitro Antimycobacterial Activity of some Isonicotinyl Hydrazones". *Bioorg Med Chem Lett*. 15:4502–4505.

20. West, D.X., A. Liberta, S.B. Padhye, R.C. Chikate, P.B. Sonawane, A.S. Kumbhar, and R.G. Yerande. 1993. *Coord. Chem. Rev*. 123: 49–71.

21. Whalen, C., C.R Horsburgh, and D. Hom. 1995. "Accelerated Course of Human

Immunodeficiency Virus Infection after Tuberculosis". *Am J Respir Crit Care Med*. 151:129-135.

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