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## SYNTHESIS, SPECTRAL CHARACTERIZATION AND EVALUATION OF *INVITRO* ANTIBACTERIAL ACTIVITY OF ISONICOTINOYL HYDRAZONES BEARING PYRIDINE MOIETY

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### ABSTRACT

Isonicotinoyl and nicotinoyl hydrazones bearing pyridine moiety have been synthesized by simple condensation reaction between carbonyl compounds(1-3) viz. 2-formyl pyridine, 2-acetylpyridine, 2-benzoylpyridine and isonicotinic acid hydrazide (4)/nicotinic acid hydrazide(5). All the hydrazones are thoroughly characterized by IR, <sup>1</sup>H- NMR and mass spectral data. Syntheses of these compounds are further confirmed by mass spectrometry. All the compounds (6-11) were screened for their anti-bacterial activities against *Staphylococcus aureus*, *Bacillus subtilis*, *Escherichia coli* and *Salmonella typhi*. Isonicotinoyl hydrazones show more antibacterial activity than the corresponding nicotinoyl hydrazones. Substituent groups -H, -CH<sub>3</sub> and C<sub>6</sub>H<sub>5</sub> groups of azomethine carbon are varied. The hydrazones having a methyl group attached to azomethine carbon atom show more pronounced activity.

**KEYWORDS:** Synthesis, characterization, isonicotinoyl and nicotinoylhydrazones, antibacterial activity.



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## INTRODUCTION

Isonicotinic acid hydrazide (INH) is the first time medication in the prevention and treatment of tuberculosis. It is one of the first antidepressive drugs discovered. It is also used in a wide range of bacterial diseases<sup>1-5</sup>. Hydrazones derived from condensation of isonicotinylhydrazine with pyridine aldehydes and ketones have been found to show better anti-tubercular activity<sup>6</sup> rather than INH. 2-hydroxynaphthaldehyde isonicotinylhydrazone<sup>7</sup> showed greater antibacterial activity against chloroquine resistant and sensitive parasites. Isonicotinoyl hydrazone, viz. N-{1-[2hydroxy-3-(piperazine-1-ylmethylphenyl) ethylidene] isonicotinylhydrazide was found to possess anti tubercular activity<sup>8</sup>. Sriram et al synthesized a new series of antimycobacterial agents containing INH group. 1-(4-Fluorophenyl)3-(4-{1-pyridine-4-carbonyl)hydrazine] ethyl} thiourea was found to be most potent compound<sup>9</sup>. Isonicotinoylhydrazones of anacardialdehydes<sup>10</sup> showed potent antimycobacterial activity against mycobacterium smegmatis mc<sup>2</sup> 155. These compounds also showed activity against mycobacterium tuberculosis H37 Rv<sup>11</sup>. Isonicotinoyl and nicotinoylhydrazones belong to the class of acylhydrazones having or (O=C) -NH- N=CR'. Acyl hydrazones are of considerable interest in the development of novel compounds with anticonvulsant, anti-inflammatory, antidepressant, analgesic, antimicrobial, antimycobacterial and anticancer activities. The increase in prevalence of multiple drug resistance has slowed down the development platform for new synthetic antimicrobial agents, and has necessitated the search for new antimicrobials compounds from alternative sources. However, studies on isonicotinoyl and nicotinoylhydrazones bearing pyridine moiety are very limited<sup>12-14</sup>. For example, pyridine-2-carboxaldehyde isonicotinylhydrazone<sup>15</sup> was used as chelating agent with iron and DNA to study the toxicity in the treatment of iron overload disease. In the view biological importance of

isonicotinoyl and nicotinoylhydrazones, to explore the effect of substituents on azomethine carbon atom and to develop chelating ligands, it was considered worthwhile to synthesize, characterize and to evaluate antibacterial activity of a series of closely related isonicotinoyl and nicotinoyl hydrazones bearing pyridine moiety. The discs impregnated with specific antibiotics or the test substances are placed on the surface of the Muller Hinton agar medium inoculated with the target organisms, which is recommended for the diffusion of antimicrobial agents as described in NCCLS approved standard. The plates are incubated and the zones of inhibition around each disc are measured.

## MATERIALS AND METHODS

Analytical grade 2-formylpyridine, 2-acetyl pyridine and 2-benzoyl pyridine were procured from Sigma-Aldrich Chemicals Pvt. Ltd. India. Isonicotinic acid hydrazide and nicotinic acid hydrazide were purchased from Merck chemicals. DMF (N,N- dimethyl formamide) , ethanol were of AR grade and used as supplied. Elemental analysis was carried out with a Perkin-Elmer 2400 CHNS/O analyzer. Mass spectra of compounds were recorded on JEOLGCMATEIIGC-Mass spectrometer in EI<sup>+</sup> ionization mode in IIT-M Chennai. IR spectra of all the hydrazones in solid state in the range of 4000-300 cm<sup>-1</sup> were recorded on a Perkin-Elmer 100 Fourier transform infrared spectrometer. <sup>1</sup>H-NMR spectra were recorded at 400.00 MHz on a Avanc-400 Bruker, Switzerland NMR spectrometer at CDRI, Lucknow.

### *Preparation of sample solution for antimicrobial activity*

With different concentrations of 5 mg, 10 mg, 20 mg, 40 mg/ml of each compound were prepared in DMF that had no influence on the microbial growth.

**Bacterial species used**

The bacteria *Staphylococcus aureus*, *Bacillus subtilis* are Gram positive *Salmonella typhi* and *Escherichia coli* are Gram negative culture of human pathogens were used to test the antibacterial activity our compounds. Nutrient agar (Bacto-beef extract 3 g; peptone 5 g; NaCl 5g; and distilled water 1000 ml) for bacteria, media chemicals present study purchased from Hi media, India. The standard bacterial strains were acquired from the Microbial Type Culture Collection (MTCC), Institute of Microbial Technology (IMTECH), and Chandigarh, India. The pure bacterial cultures were maintained on Nutrient Agar Media (NAM).

**Synthesis of 2-Formylpyridine isonicotinoylhydrazone (FPINH) (6)**

A 5 mmol of 2-formylpyridine (0.55 ml) dissolved in 20ml of methanol was added to an methanolic solution of 5 mmol of isonicotinic acid hydrazide (0.68g). The contents were taken in a round bottom flask stirred for 20 min. A white coloured product was formed. It was collected by filtration, washed with a few drops of ethanol and dried in vacuum. Yield of the product is 85%, M.P, 158-160°C, elemental analysis: C-63.71(63.42); H-4.42 (4.81); N: 24.77(24.98); IR spectra; 3294, 1668, 1542 cm<sup>-1</sup> are assigned to  $\nu(\text{NH})$ ,  $\nu(\text{C=O})$  and  $\nu(\text{C=N})$  stretching vibrations respectively. <sup>1</sup>H-NMR spectra in DMSO solvent,  $\delta$  (7.69-8.01) (multiplet 4H),  $\delta$  (8.69) (multiplet 4H),  $\delta$ (8.15) (singlet 1H),  $\delta$ (12.25) (singlet 1 H), are respectively assigned to pyridine, isonicotinic, -NH and aldehydic proton. GC-MS spectrum of FPINH shows molecular ion peak at (*m/z*) 226.

**Synthesis of 2-Acetylpyridine isonicotinoylhydrazone (APINH) (7)**

2-Acetylpyridine (0.60 ml, 5 m mol) dissolved in 20 ml of ethanol was added to an ethanolic solution of isonicotinic acid hydrazide (0.68g, 5 m.mol). The contents were taken in a round bottom flask and refluxed over water bath for 2-3 hrs. On cooling the contents, a white coloured product was formed. It was collected by filtration, washed with few drops of ethanol and dried in vacuum. The yield of the product is

82%, M.P, 162-164°C, Elemental analysis: C-65 (65.02); H-5 (5.06); N: 23.33(23.56); IR spectra; 3189, 1668, 1581 cm<sup>-1</sup> are assigned to  $\nu(\text{NH})$ ,  $\nu(\text{C=O})$  and  $\nu(\text{C=N})$  stretching vibrations respectively. <sup>1</sup>H-NMR spectra in DMSO solvent.  $\delta$  (3.34) (singlet 3H),  $\delta$  (7.36-7.62) (multiplet 4H),  $\delta$ (8.13) (singlet 1H),  $\delta$ (8.63-8.94) (multiplet 4H), are respectively assigned to methyl, pyridine, -NH and isonicotinic. GC-MS spectrum of APINH shows molecular ion peak at (*m/z*) 240.

**Synthesis of 2-Benzoylpyridine isonicotinoylhydrazone (BPINH)(8)**

A 5 m.mol of 2-benzoyl pyridine (0.91 g) dissolved in 20ml of ethanol was added to an ethanolic solution of 5 m.mol of isonicotinic acid hydrazide (0.68gms). The contents were taken in a round bottom flask and 3-4 drops of glacial acetic acid added to it and refluxed for 2-3 hrs on water bath. The contents were cooled and filtered. On evaporation of the solvent a light yellow coloured crystalline product was formed. The yield of the product is 76%, M.P-186-188°C, Elemental analysis: C-71.52 (71.86); H-4.63 (4.83); N: 18.54(18.64); IR spectra; 3434, 1690, 1578 cm<sup>-1</sup> are assigned to  $\nu(\text{NH})$ ,  $\nu(\text{C=O})$  and  $\nu(\text{C=N})$  stretching vibrations respectively. <sup>1</sup>H-NMR spectra in DMSO solvent.  $\delta$  (7.41-7.78) (multiplet 4H),  $\delta$  (7.52-7.67) (multiplet 5H),  $\delta$ (8.04-8.83) (multiplet 4H),  $\delta$ (8.98) (singlet 1H), are respectively assigned to pyridine, phenyl ring protons, isonicotinic and -NH. GC-MS spectrum of BPINH shows molecular ion peak at (*m/z*) 302.

**Synthesis of 2-Formylpyridine nicotinoylhydrazone (FPNH) (9)**

A 5 m.mol of 2-formylpyridine (0.55 ml) dissolved in 20 ml of methanol was added to a methanolic solution of 5 mmol of nicotinic acid hydrazide (0.68 g). The contents were taken in a 250-ml round bottom flask and refluxed over water bath for 2 hrs. The contents were cooled and filtered. On evaporation of the solvent a light white coloured crystalline product was formed, washed with a few drops of ethanol and dried in vacuum. The yield of the product is 86%, M.P, 106-108°C, elemental analysis: C-

63.71(63.42); H-4.42 (4.81); N: 24.77(24.98); IR spectra; 3496, 1670, 1591  $\text{cm}^{-1}$  are assigned to  $\nu$  (NH),  $\nu$ (C=O) and  $\nu$ (C=N) stretching vibrations respectively.  $^1\text{H-NMR}$  spectra in  $\text{CDCl}_3$  solvent.  $\delta$  (7.39-7.59) (multiplet 4H),  $\delta$  (8.57) (singlet 1H),  $\delta$ (8.73-8.81) (multiplet 4H),  $\delta$ (11.01) (singlet 1 H), are respectively assigned to pyridine, -NH, nicotine, and aldehydic proton. GC-MS spectrum of FPNH shows molecular ion peak at ( $m/z$ ) 226.

#### **Synthesis of 2-Acetylpyridine nicotinoylhydrazone (APNH) (10)**

A 5 m.mol of 2-acetyl pyridine (0.60 ml) dissolved in 20 ml of ethanol were added to an ethanolic solution of 5 m.mol of nicotinic acid hydrazide (0.68gms). The contents were taken in a 250-ml round bottom flask and refluxed on water bath 2-3 hrs. On cooling the contents a white coloured product was formed. It was collected by filtration, washed with few drops of ethanol and dried in vacuum. The yield of the product is 78%, M.P, 174-176 $^{\circ}\text{C}$ , Elemental analysis: C-65 (65.02); H-5 (5.06); N: 23.33(23.56); IR spectra; 3211, 1662, 1581  $\text{cm}^{-1}$  are assigned to  $\nu$ (NH),  $\nu$ (C=O) and  $\nu$ (C=N) stretching vibrations respectively.  $^1\text{H-NMR}$  spectra in  $\text{CDCl}_3$  solvent.  $\delta$  (2.52-2.56) (singlet 3H),  $\delta$  (7.43-7.82) (multiplet 4H),  $\delta$ (8.24-8.77) (multiplet 4H),  $\delta$ (9.58) (singlet 1H), are respectively assigned to methyl, pyridine, nicotine and -NH. GC-MS spectrum of APNH shows molecular ion peaks at ( $m/z$ ) 240.

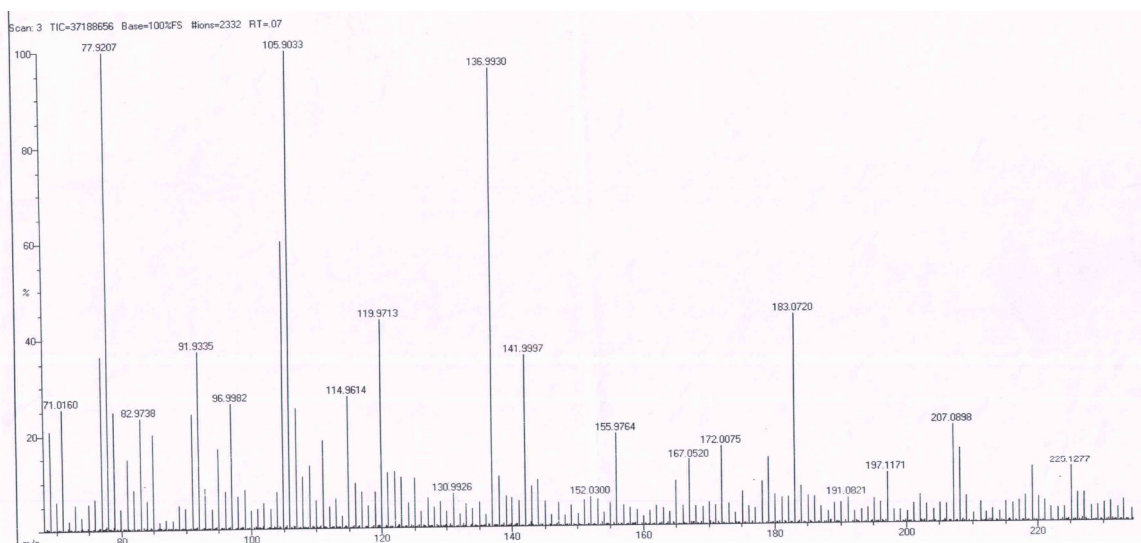
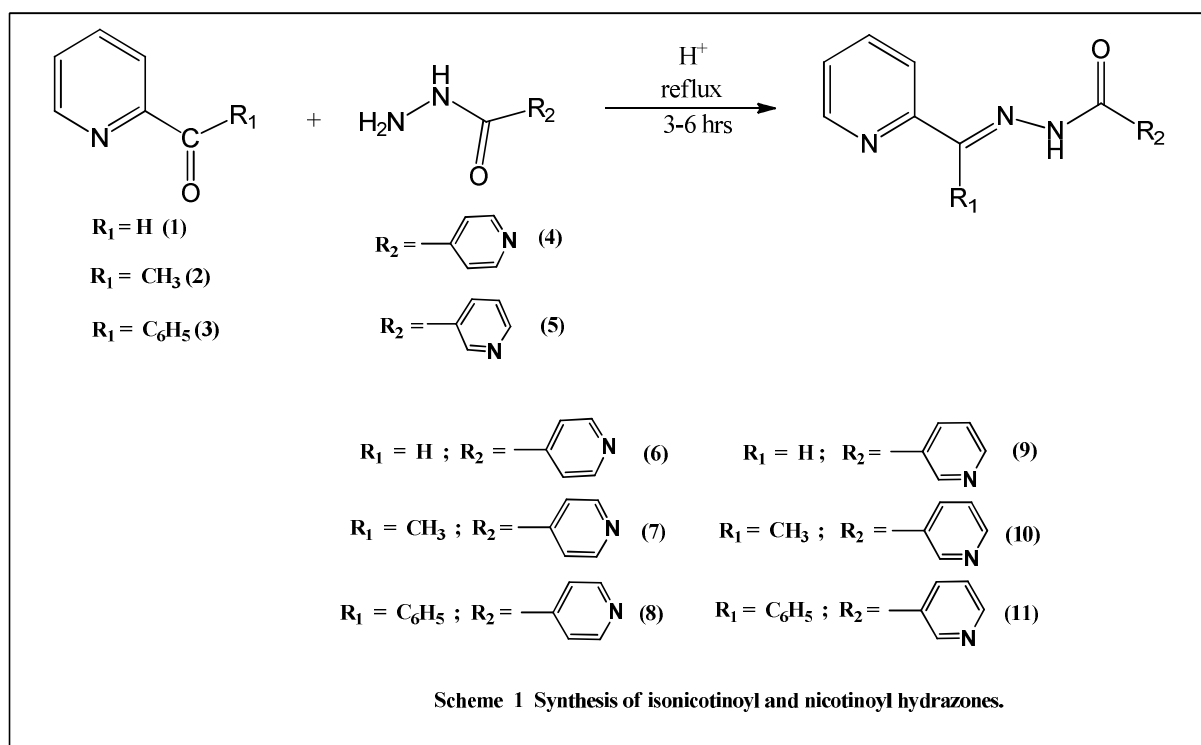
#### **Synthesis of 2-Benzoylpyridine nicotinoylhydrazone (BPNH) (11)**

A 5 m.mol of 2-benzoyl pyridine (0.91 gm) dissolved in 20ml of ethanol were added to an

ethanolic solution of 5 m.mol of nicotinic acid hydrazide (0.68 g). The contents were taken in 250-ml a round bottom flask and there drops of glacial acetic acid was added to it and refluxed for 3-4 hrs on water bath. The contents were cooled and filtered. On evaporation of the solvent a light green coloured crystalline product was formed. The yield of the product is 73%, M.P,138-140 $^{\circ}\text{C}$ , Elemental analysis: C-71.52 (71.86); H-4.63 (4.83); N: 18.54(18.64); IR spectra; 3352, 1691, 1577  $\text{cm}^{-1}$  are assigned to  $\nu$ (NH),  $\nu$ (C=O) and  $\nu$ (C=N) stretching vibrations respectively.  $^1\text{H-NMR}$  spectra in  $\text{CDCl}_3$  solvent;  $\delta$  (7.37-7.62) (multiplet 4H),  $\delta$  (7.83-7.93) (multiplet 5H),  $\delta$ (8.03-8.37) (multiplet 4H),  $\delta$ (9.18) (singlet 1H), are respectively assigned to pyridine, phenyl ring protons, nicotine and -NH. GC-MS spectrum of BPNH shows molecular ion peaks at ( $m/z$ ) 302.

## **RESULTS AND DISCUSSION**

A novel series of isonicotinoyl and nicotinoylhydrazones (6-11) are synthesized and characterized for the first time. Syntheses of hydrazones are shown in the Scheme 1. The compounds (6-11) were synthesized by simple condensation of carbonyl derivatives viz . 2-formyl pyridine(1), 2- acetylpyridine(2) and 2-benzoylpyridine(3) with isonicotinic acid hydrazide (4)/ nicotinicacid hydrazide (5). All the hydrazones are characterized by IR, NMR and mass spectral data. Spectral data (see Materials and Methods) confirm the syntheses of hydrazones (6-11). Typical mass spectra of 2-formylpyridine isonicotinoylhydrazone (6, FPNH) is given in Figure 1.



**Figure 1**  
**Mass spectrum of FPINH**

### **Biological evaluation**

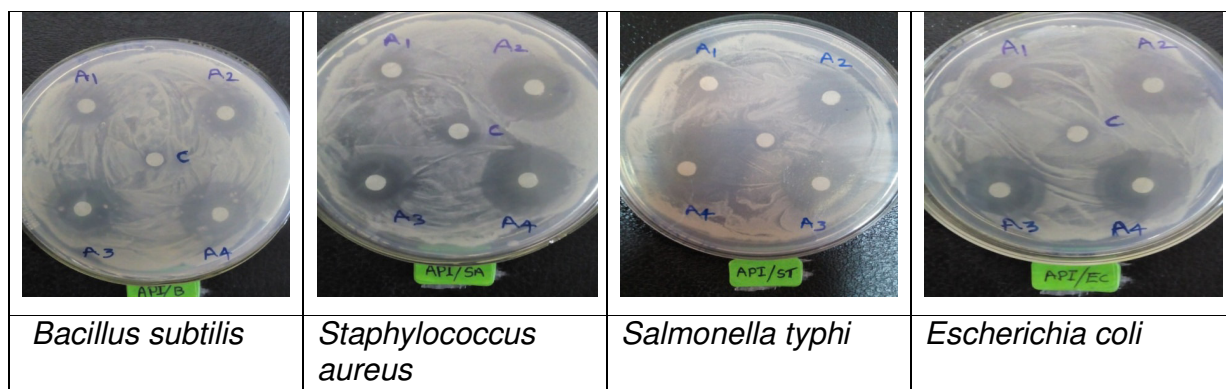
#### **Antibacterial assay**

The antibacterial activity of hydrazones were screened against the *Bacillus subtilis* (MTCC-441) and *Staphylococcus aureus* (MTCC-3160) which are gram positive and *Salmonella typhi* (MTCC-735) and *Escherichia coli* (MTCC-1652) which are gram negative organisms. Here DMF is tested as reference to assess extent of pure

inhibition of our compounds. Muller Hinton Agar plates were prepared by test microorganisms with MC Furland standards (1 to 5 x 10<sup>8</sup> cfu/ml) were inoculated by the spread plate method. Filter paper discs approximately 6 mm in diameter were soaked indifferent concentrations of tested compounds and placed in the previously prepared agar plates. Each disc was pressed down to ensure

complete contact with the agar surface and distributed evenly so that they are no closer than 24 mm from each other, center to center. The agar plates were then incubated at 37°C. After incubation, each plate was examined. The resulting zones of inhibition were uniformly

circular with a confluent lawn of growth. Typical photographs of agar plates showing antibacterial activity of APINH are given Figure 2. The diameters of the zones of complete inhibition were



**Figure 2**  
**Typical photographs of agar plates showing antibacterial activity of APINH**  
**[Here, c means control; A<sub>1</sub>- 5 mg , A<sub>2</sub> -10mg, A<sub>3</sub>-20mg, A<sub>4</sub>-40 mg/ml]**

measured and given in the Tables 1 and 2 including the diameter of the disc (NCCLS, 1997 or CLSI, 1997) (National Committee on Clinical Laboratory Standards or Clinical and Laboratory Standards Institute).

**Table 1**  
**Antibacterial activity of a group of closely related isonicotinoyl hydrazones**

Name of the Organisms	FPINH				APINH				BPINH			
	Zone of Inhibition(mm)				Zone of Inhibition(mm)				Zone of Inhibition (mm)			
	A <sub>1</sub>	A <sub>2</sub>	A <sub>3</sub>	A <sub>4</sub>	A <sub>1</sub>	A <sub>2</sub>	A <sub>3</sub>	A <sub>4</sub>	A <sub>1</sub>	A <sub>2</sub>	A <sub>3</sub>	A <sub>4</sub>
<i>B.subtilis</i>	—	—	14	15	17	20	25	28	23	28	25	25
<i>S. aureus</i>	09	09	13	20	13	25	20	26	25	23	24	21
<i>S.typhi</i>	11	22	17	20	16	20	26	30	27	25	30	24
<i>E. coli</i>	09	13	13	18	10	25	23	25	20	21	26	24

Here A<sub>1</sub>- 5 mg , A<sub>2</sub> -10mg, A<sub>3</sub>-20mg, A<sub>4</sub>-40 mg/ml and dots lines indicate negative results

**Table 2**  
**Antibacterial activity of a group of closely related nicotinoyl hydrazones**

Name of the Organisms	FPNH				APNH				BPNH			
	Zone of Inhibition(mm)				Zone of Inhibition(mm)				Zone of Inhibition(mm)			
	A <sub>1</sub>	A <sub>2</sub>	A <sub>3</sub>	A <sub>4</sub>	A <sub>1</sub>	A <sub>2</sub>	A <sub>3</sub>	A <sub>4</sub>	A <sub>1</sub>	A <sub>2</sub>	A <sub>3</sub>	A <sub>4</sub>
<i>B.subtilis</i>	08	11	08	14	---	15	20	21	---	10	16	19
<i>S. aureus</i>	09	11	11	14	15	17	19	21	09	12	23	25
<i>E. coli</i>	13	10	11	14	07	13	19	22	09	12	30	28
<i>S.typhi</i>	10	11	15	20	13	19	21	22	15	20	23	25

Here A<sub>1</sub>- 5 mg , A<sub>2</sub>-10mg, A<sub>3</sub>-20mg, A<sub>4</sub>-40 mg/ml and dots lines indicate negative results

The antibacterial activities of our compounds are comparable to the activity of standard drug Streptomycin (*S. aureus*- 30mm, *B.subtilis*-28 mm, *E.coli*- 34mm, *S.typhi*- 24mm). Isonicotinoyl hydrazones (INHs) show more activity when compared with nicotinoyl hydrazones (NH) compounds. Among INH compounds, APINH show more activity than BPNH and finally FPNH. At low concentrations, FPNH, APNH, BPNH do not inhibit one of the Gram-positive bacteria (*B.subtilis*) and it is the index for low MIC (Minimum Inhibitory Concentration). All the compounds show gradual increasing activity with an increase in concentrations towards both gram positive and gram negative bacterial species but at maximum concentrations show low activity due to less diffusion rate in agar medium. Isonicotinoyl hydrazones show more antibacterial activity than the corresponding nicotinoyl hydrazones. Substituent groups - H, -CH<sub>3</sub> and C<sub>6</sub>H<sub>5</sub> groups of azomethine carbon are varied. The hydrazones having methyl group attached to azomethine carbon atom show more pronounced activity. In our present study we are investigating our compounds which are more antibacterial in

nature and it makes platform for preparation of effective chemotherapeutics agents for therapy of human pathogenic diseases.

## CONCLUSION

We have synthesized and characterized a new series of closely related isonicotinoyl and nicotinoyl hydrazones bearing pyridine moiety and evaluated their anti-bacterial activity. Isonicotinoyl hydrazones show more antibacterial activity than the corresponding nicotinoyl hydrazones. Substituent groups, H, -CH<sub>3</sub> and C<sub>6</sub>H<sub>5</sub> groups of azomethine carbon are varied. The hydrazones having methyl group attached to azomethine carbon atom show more pronounced activity.

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## REFERENCES

1. Fox H.N, The chemical approach to the control of tuberculosis, *Science*, 116, 129 (1952).
2. Mazza P, Orcesi M, Pelizzi C , , Pelizzi G, Predieri G and Zaini F, Synthesis, structure, antimicrobial, and genotoxic activities of organotin compounds with 2,6-diacetylpyridine nicotinoyl- and isonicotinoylhydrazones , *Journal of Inorganic Biochemistry*, 48, 251 (1992).
3. Ianelli S, Mazza P, Orcesi M, Pelizzi C Pelizzi G, Predieri G and Zaini F, Synthesis, structure and biological activity of organotin compounds with di-2-pyridylketone and phenyl (2-pyridyl)ketone -2-aminobenzoyl hydrazone,*Journal of Inorganic Biochemistry*, 60, 89 (1995).
4. Cesur Z, Buyuktimkin n, Derbentli S, Synthesis and antimicrobial evaluation of some aroylhydrazones of 4-[(2-Methylimidazo[1,2-a]pyridine-3yl)azo] benzoic acid hydrazide. *Archiv der Pharmazie*, 323, 41 (1990).
5. Bottari B , Maccari R, Monforte F, Ottana r, Rotondo E, Vigorita MG, Isoniazid related copper(II) and nickel(II) complexes with antimycobacterial *in vitro* activity, *Bioinorganic Medicinal Chemistry Letters*, 10, 657 (2000).
6. Rollas S and Güniz S. K., Biological Activities of Hydrazone Derivatives, *Molecules*, , 12, 1910 (2007).
7. Richardson DR, Bernhardt PV, , Crystal and molecular structure of 2-hydroxy-1-naphthaldehyde isonicotinoyl-hydrazone(NIH) and its iron(III) complex an iron chelator with anti-tumour activity, *J Biol. Inorg. Chem.*, 4, 266(1999).
8. Walcourt A, Loyevsky M, Lovejoy DB, Gordeuck V.R, Richardson D.R , Novel aroylhydrazone and thiosemicarbazone iron chelators with anti-malarial activity against chloroquine-resistant and -sensitive parasites. *Int J Biochem Cell Biol.* 36, 401 (2004).
9. Sriram D, Yogeewari P , Madhu K.. Synthesis and *in vitro* and *in vivo* antimycobacterial activity of isonicotinoyl hydrazones, *Bioorg. Med. Chem Lett.* 15, 4502 ( 2005).
10. Sriram D, Yogeewari P. Madhu K. Synthesis and in vitro antitubercular activity of some 1-[4- sub]phenyl]-3-(4(1-[(pyridine-4-carbonyl hydrazone]ethyl)phenylthiourea, *Bioorg. Med. Chem.*, 14, 876 (2006)
11. Narayana Swamy B. T. K. Suma, G. Venkateswara Rao, G. Chandrasekara Reddy, Synthesis Of isonicotinoyl hydrazones from anacardic acid and their *in vitro* activity of against *mycobacterium smegmatis*, *Eur.J Med. Chem .*, 42, 420.(2007).
12. Nataliya P. Belskaya, Wim Dehaen and Vasiliy A. Bakuleva Synthesis and properties of hydrazones bearing amide, thioamide and amidine functions, *Arkivoc.* 2010, 275( 2010)
13. M.M.E Shakdofa, , M.H. Shtaiwl, N. Morsy and T.M.A. Abdul-Rassel, Metal complexes of hydrazones and their biological, analytical and catalytic applications: A review *Main Group Chemistry*, 13, 187 (2014).
14. Xin Su and Ivan Aprahamian, Hydrazone –based switches, metallo assemblies and sensors, *Chem . Soc. Reviews*, 43, 1963 (2014).
15. Chaston TB, Richardson DR. interaction of the pyridine -2- carboxaldehyde isonicotinoylhydra- zone class of chelators with iron and DNA implications for toxicity in the treatment of iron overload diseases, *J. Biol . Inorg Chem.* 8, 427 (2003).