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SYNTHESIS AND BIOLOGICAL EVALUATION OF ISONIASID DERIVATIVES

R.Saraswathi[1], Lokesh Upadhyay[2], C.Vijaya[3], R.Venkatakrishnan[4]

[1]Al –Shifa College of Pharmacy, Kerala , [2]Sastra University, Tanjore, [3]Dean and HOD of Pharmaceutics, Ultra Misson and Research Centre, [4]Ultra College of Pharmacy, Madurai, Research Scholar , Sastra university, Tanjore, Madurai ,TamilNadu, India.

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For Correspondence:

R.Venkatakrishnan

Ultra College of Pharmacy, Madurai

E-mail:

meeraharsa@yahoo.com

ABSTRACT

Aldehydes and ketones (three analogues) were synthesized and evaluated for physicochemical characterization & scanned for the antibacterial activity all the synthesized compounds were most active than the INH and the compound KRA3 was most active Analogue. Synthesized compounds (KRA1, KRA2, KRA3) were characterized based on spectral data and physical constant and evaluated for anti-bacterial activity in vitro using various micro-organisms. Amikacin was used as a standard. The compounds KRA2 & KRA3 were most active against *E.Coli, Staphylococcus aureus, Pseudomonas aerugenosa* inactive against *Proteus vulgaris and Klebsiella.*

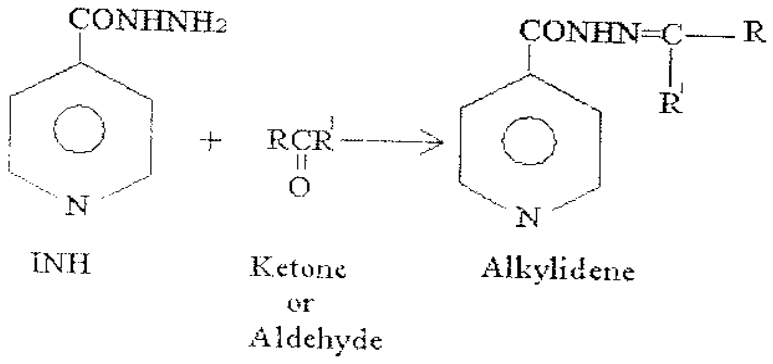
INTRODUCTION

Isoniasid is one of the Anti-tubercular drug humanity is a leading infectious disease, known to around the world despite the introduction of a chemotherapy in the mid 1940's. The discovery of the tuberculostatic activity of Isoniasid and its derivatives plays a major role in the treatment of tuberculosis. Isoniasid and its derivatives show a wide spectrum of pharmacological activities such as anti tubercular and preventive therapy in HIV patients[1,2,3]. In the structure activity relationship studies of Isoniasid, a number of derivatives have been prepared using the hydroxide group, either by way of substitution or condensation or introduction of a heterocyceling extension of the work on the Nicotinamide analogues has led to the discovery of other Anti-tubercular compounds. So the prepare Anti tubercular compounds involving the molecules different from INH with better Activity[4,5,6].

MATERIALS AND METHODS

The compounds were all white crystalline powder has no odour. Melting points were determined by open capillary tube method and the values are given in Table -1 all the synthesized derivatives of INH were subjected to solubility testing of the results are given in the table -2. IR Spectra were recorded on Perkins -Elmer 577 IR Spectrophotometer using KBR pallet technique. Only sharply defined 1R peaks are reported. All the synthesized compounds showed Antibacterial activity against all pathogenic species, like *E.coli, Staphylococcus albus, pseudomonas aeruginosa.*

Experimental work



KRA1-1-Isonicotinyl 2 (1-disphenyl methylidene hydroxide)

Equimolar quantities (0.01 mol) of isonicotinyl hydroxide (1.3714gms) and benxophenone (1.24ml) were refluxed two hours in ethanol (20ml) in the presence of 2-3 drops of glacial Acetic acid. The reaction mixture was then kept in the ice cold water and the product was obtained by filtration. Then it is recystallised from ethanol.

KRA2-a-isonicotinyl 2 (1-dimethyl amino benxylidens) hydraoxide

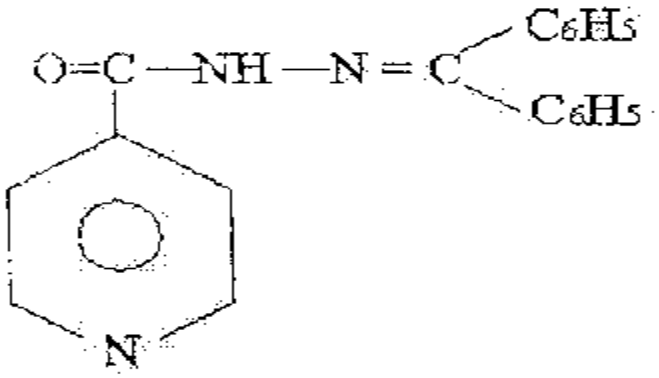
Equmiolar quantitites (0.01mol) of isonicotinyl hydraoxide (1.3714 gms0 and 4-dimethl amino benxaldehyde (2.040ml) were refluxed for 2 hours in ethanol (20ml) in the presence of 2-3 drops of glacial Acetic acid. The reaction mixture was then kept in ice-cod water and the product was obtained by filtration. It is crystallized from ethanol.

KRA3-1- Isonicotinyl 2-(1-ethylidine) hydroxide

Equimolar quantities (0.01mol) of isonicotinyl hydroxide (1.3714gms) and acetaldehyde (1.1ml) were refluxed for 2 hours in ethanol 25ml in the presence of 2-3 drops of glavial acetic acid. Then the product was obtained by filtration. It is recrstallized from ethanol.

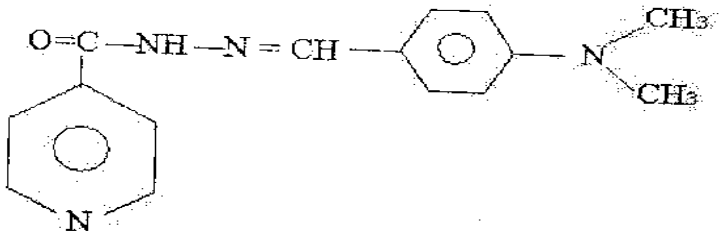
Analytical work[7,8,9]

KRA1-1- isonicotinyl 2(1-diphenyl methylidene hydraoxide



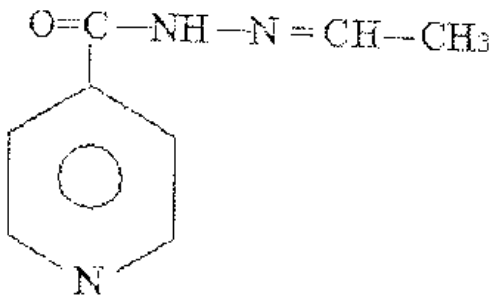
3100 (N-H stre), 3020 (C-H stre-Ar), 1670-1650 (>C=N-stre)1630 (C=0 stre), 1540 {-C=C-}stre in ring = Ar{-C=N-}1450 -1060 (Ar.C-H stre), 730 (C-H def)

KRA2-1-isonicotinyl 2 (1-diphenyl methylidene hydraoxide



3100 (N-Hstre), 3040 (C-H stre-Ar), 1660-(>0 = N-stre) ,1310 (3 amines-C-N-stre), 1630 (>C=N-stre), 820 (Ar.parasubstituted C-H def), 730 (C-H def), 630-780 (C-H def-disubstituted Ar)

KRA3-1-isonicotinyl 2 (1-dimethyl animo benxylidene hydraoxide



3290 (NH group stre-sec), 3020 (Ar-C-H stre), 2880 [(C-H stre (Almane)], 1650 (>C=N-stre), 1630 (>C=0-stre), 1540 = {-CH_3} deformation,, 1810 {(C-N stre (3^0 amnies){C-H}

Anti bacterial Activity[10,11,12,13]

Isonicotinic Acid hydroxide and the synthesized compounds were screened for anti-bacterial activity against the pathogenic species.

Media used – Mullor Hinton Agar (Hi-media)

Method – agar dilution

Organism tested – *Salmonella typhi, Klebsiella, protects valugairs, staphylococeus aureaus, E.Coli, Stephylococus albas, pseudomonas aeruaginosa.* The medium was

prepared and allowed to cool at 50°c. The concentration of the test sample used were from 5000Mg/ml to lower concentration made by serial double dilutions with suitable solvents. Then these were distributed in the different plates. Then inoculate the organism and allowed to incubate over night at 350°c. The minimum inhibitory concentration (M/C) was taken as the lowest concentration (higher dilution) without visible growth. The zone of inhibition of 110H of the synthesized compounds tested are shown in the table -3

RESULTS AND DISCUSSION

Synthesized compounds (KRA1, KRA2, KRA3) were characterized based on spectral data and physical constant and evaluated for anti-bacterial activity in vitro using various micro-organisms. Amikacin was used as a standard. The compounds KRA2 & KRA3 were most active against *E.Coli, Staphylococcus albus, pseudomonas aeruigenosa* inactive against *proteus vulgaris* and *Klebsiella.*

Table 1

Physical characters of the synthesized compounds

Compound Code	Melting Point(°c)	Yield (%)	Mol Formula	Mol Wt
KRA_1	**168-170**	**82**	**$C_{19}N_3H_{15}O$**	**291**
KRA_2	**172-173**	**74**	**$C_{15}N_4H_{16}O$**	**258**
KRA_3	**156-158**	**65**	**$C_8N_3H_9O$**	**163**

Table 2

Anti bacterial activity of the synthesized compounds

S.no	Microorganisms	KRA_1	KRA_2	KRA_3	INH	Amikacin
1.	*S.typhi*	-	-	11 mm	-	21 mm
2.	*Klb.pneumoniae*	-	-	-	7 mm	20 mm
3.	*P.vulgaris*	-	-	-	-	21 mm
4.	*S.aureus*	-	11 mm	-	-	10 mm
5.	*E.coli*	10mm	11 mm	14 mm	8 mm	18 mm
6.	*S.albus*	8 mm	13 mm	9 mm	-	10 mm
7.	*Pseudomonas aeuriginosa*	-	-	16 mm	-	19 mm

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