Available online at www.sciencedirect.com

SciVerse ScienceDirect

journal homepage: www.elsevier.com/locate/jopr

Original Article

Synthetic, structural and pharmacological studies on some isonicotinohydrazide and benzohydrazide analogues

S. Syed Tajudeen [a], Geetha Kannappan [b,*]

[a] Assistant Professor & Head, Department of Chemistry, Aalim Muhammed Salegh College of Engineering, Avadi-IAF, Chennai 600 055, Tamil Nadu, India

[b] Associate Professor & Head, PG & Research Department of Chemistry, Muthurangam Government Arts College, Vellore 632 002, Tamil Nadu, India

ARTICLE INFO

Article history:
Received 6 June 2013
Accepted 24 June 2013
Available online 17 July 2013

Keywords:
Anti-mycobacterial
Benzhydrazide
Isoniazid
Mycobacterium tuberculosis
Schiff base

ABSTRACT

Aim: A series of new isonicotinohydrazide and benzohydrazide analogues were synthesized by conventional one pot reaction of isoniazid and benzhydrazide with various disubstituted benzaldehydes in ethanol.

Methods: The isonicotinohydrazide and benzohydrazide derivatives were prepared by the reaction between the corresponding substituted benzaldehyde (10 mmol) with isoniazid and benzhydrazide (10 mmol) in ethanol (30 mL).

Results: The synthesized compounds were characterized by Elemental analyses, LC-MS, FT-IR, ^{1}H NMR and ^{13}C NMR and evaluated for their *in vitro* antimicrobial activity against *Mycobacterium tuberculosis* **$H_{37}Rv$** (MTB).

Conclusion: The syntheses of the 12 derivatives were performed. In relation to the biological studies, it was found that the compounds A6 and C6 showed higher activity against all the tested bacterial strains and the compounds A1–A6 exhibited the highest efficacy and exhibited >70% inhibition against the *M. tuberculosis*.

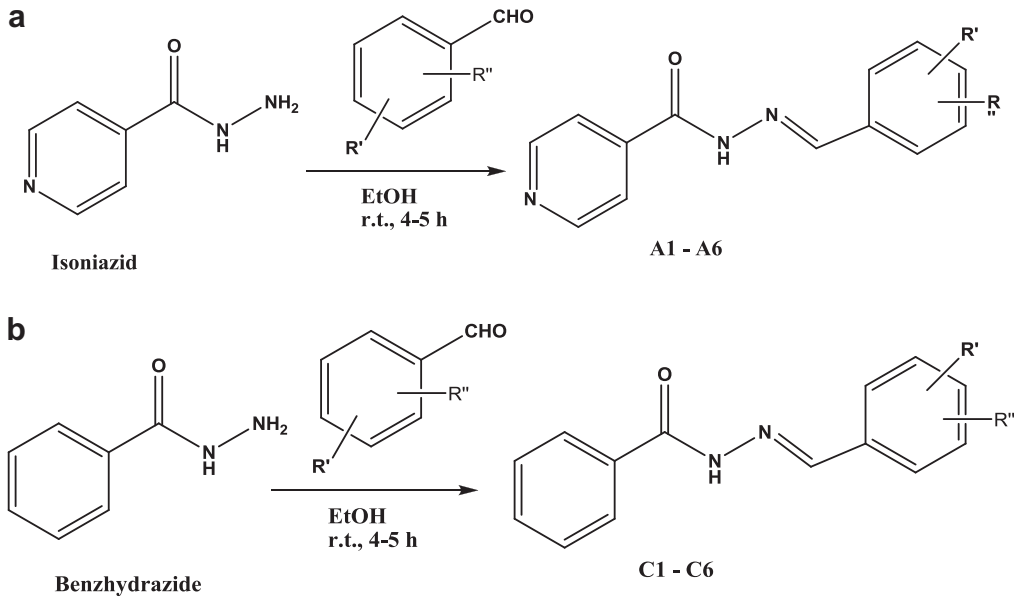
Copyright © 2013, JPR Solutions; Published by Reed Elsevier India Pvt. Ltd. All rights reserved.

1. Introduction

Tuberculosis is a chronic bacterial infection, voices the World Health Organization[1–3] and caused by a bacterium called *Mycobacterium tuberculosis*. In many parts of the world, the limitation is to use the combination of only five drugs to treat TB effectively, namely rifampicin (RIF), isoniazid (1NH), ethambutol (ETH), streptomycin (STR) and pyrazinamide (PZA). Limitations involved in the chemotherapy of tuberculosis are because of secondary line drugs such as ethionamide, aminosalicylic acid, cycloserine, amikacin, kanamycin and capreomycin are toxic in nature and cannot be employed simultaneously.[4] The reemergence of TB infection is further complicated by an increase in cases, which are resistant to conventional antitubercular drug therapy.[5] On the other hand, in spite of toxicity on repeated dosing, isoniazid (1NH) is still considered a first-line drug for chemotherapy of tuberculosis.[6]

There are two basic approaches to develop a new drug for TB: (a) synthesis of analogues and modifications are derivatives of existing compounds for shortening and improving

* *Corresponding author*. Tel.: +91 9486925596.
E-mail addresses: senthil_geetha@rediffmail.com, geetha.mgac@gmail.com (G. Kannappan).
0974-6943/$ – see front matter Copyright © 2013, JPR Solutions; Published by Reed Elsevier India Pvt. Ltd. All rights reserved.
http://dx.doi.org/10.1016/j.jopr.2013.06.017



A1 & C1 R'= H R''= H
A2 & C2 R'= 2-OCH_3, R''= 3-OCH_3
A3 & C3 R'= 2-OCH_3, R''= 4-OCH_3
A4 & C4 R'= 2-OCH_3, R''= 5-OCH_3
A5 & C5 R'= 3-OCH_3, R''= 4-OCH_3
A6 & C6 R'= 3-OCH_3, R''= 5-OCH_3

Scheme 1 – a) Synthetic route used for the preparation of isoniazid derivatives A1-A6. b) Synthetic route used for the preparation of benzhydrazide derivatives C1-C6. Isonicotinoyl hydrazones and benzohydrazide, considered medicinally important, is microwave-assisted, environment friendly, high yielding and time saving synthesis. It was carried out by the condensation of isoniazid (1NH) and benzhydrazide (BZA) with disubstituted benzaldehydes under the solvent-free conditions without any solid support. The synthesized hydrazones were structurally characterized by LC-MS, Elemental analyses, FT-IR, ^{1}H NMR and ^{13}C NMR and evaluated for their in vitro antibacterial activity against *Mycobacterium tuberculosis* $H_{37}Rv$ using BACTEC 460 radiometric system.

Table 1 – Analytical and physico-chemical data of hydrazones.

Compound	Empirical formula	LC/MS (m/e)	Log P[a]	Elemental analysis found (Calcd) (%)		
				C	H	N
A1	$C_{13}H_{11}N_3O$	226	2.03	69.49 (69.32)	4.93 (4.92)	18.76 (18.65)
A2	$C_{15}H_{15}N_3O_3$	286	1.77	62.86 (63.14)	5.36 (5.30)	14.70 (14.73)
A3	$C_{15}H_{15}N_3O_3$	286	1.77	62.13 (63.14)	5.22 (5.30)	14.55 (14.73)
A4	$C_{15}H_{15}N_3O_3$	286	1.77	62.92 (63.14)	5.14 (5.30)	14.61 (14.73)
A5	$C_{15}H_{15}N_3O_3$	286	1.77	62.52 (63.14)	5.24 (5.30)	14.51 (14.73)
A6	$C_{15}H_{15}N_3O_3$	286	1.77	62.76 (63.14)	5.20 (5.30)	14.68 (14.73)
C1	$C_{14}H_{12}N_2O$	225	3.36	73.31 (74.98)	6.15 (5.39)	12.19 (12.49)
C2	$C_{16}H_{16}N_2O_3$	285	3.11	67.60 (67.59)	6.97 (5.67)	9.77 (9.85)
C3	$C_{16}H_{16}N_2O_3$	285	3.11	66.60 (67.59)	7.97 (5.67)	9.75 (9.85)
C4	$C_{16}H_{16}N_2O_3$	285	3.11	67.10 (67.59)	6.37 (5.67)	9.23 (9.85)
C5	$C_{16}H_{16}N_2O_3$	285	3.11	67.05 (67.59)	6.25 (5.67)	9.15 (9.85)
C6	$C_{16}H_{16}N_2O_3$	285	3.11	66.30 (67.59)	6.17 (5.67)	9.28 (9.85)
Isoniazid	–	–	−0.6			
Benzohydrazide	–	–	0.21			

a Calculated using the programs CS ChemOffice, ChemDraw Ultra ver. 11.0 (CambridgeSoft, Cambridge, MA, USA).

Download English Version:

https://daneshyari.com/en/article/8541627

Download Persian Version:

https://daneshyari.com/article/8541627

Daneshyari.com