International Journal of Research and Development in Pharmacy and Life Sciences
Available online at http//www.ijrdpl.com
February - March, 2014, Vol. 3, No.2, pp 905-908
ISSN: 2278-0238

Research Article

ANTIOXIDANT ACTIVITY OF NOVEL 4-OXO-AZETIDINE DERIVATIVES SYNTHESIZED FROM SCHIFF BASES

N. Madhavi*, B. Lourdu Rani

Department of Chemistry, JKC College, Guntur-522002.

***Corresponding Author: Email bhavanam.chem@gmail.com**

(Received: November 21, 2013; **Accepted:** January 27, 2014**)**

ABSTRACT

The synthesized 4-Oxo-Azetidines which are established by spectral and analytical data are evaluated for their antioxidant activity. The activity of all compounds is identified by using nitricoxide and superoxide radical scavenging methods against Alkaline Dimethyl Sulphoxide (DMSO). The derivatives with chlorine substituent either at ortho or para on phenyl ring exhibited maximum activity in both methods. Least activity is shown by the compound having ortho nitro group on benzene ring.

Keywords: *4-Oxo- Azetidine, Schiff base, Antioxidant activity*.

INTRODUCTION

4-oxo-Azetidines are 4-membered cyclic amides derived from Schiff bases which contain β-lactam unit as an essential structural feature of its molecule[1]. Monocyclic Azetidinones are usually referred to as Azetidin-2-ones or 2-oxo azetidine, based on the nomenclature of parent heterocycle, Azetidine. The utility of 4-oxo-Azetidines as synthons for various biologically active compounds, as well as their recognition as cholesterol absorption inhibitors and enzyme inhibitors has given in various studies[2,3].

Free radicals are types of Reactive Oxygen Species (ROS), which include all highly reactive oxygen containing molecules[4,5]. They are capable of attacking the healthy cells of the body, causing them to lose their structure and function. Cell damage caused by the free radicals appears to be a major contribution to aging and degenerative disease of aging such as cancer, cardiovascular diseases, cataract, immune system decline, liver disease, diabetes mellitus, inflammation, renal failure and brain dysfunction [6,7].

EXPERIMENTAL WORK:

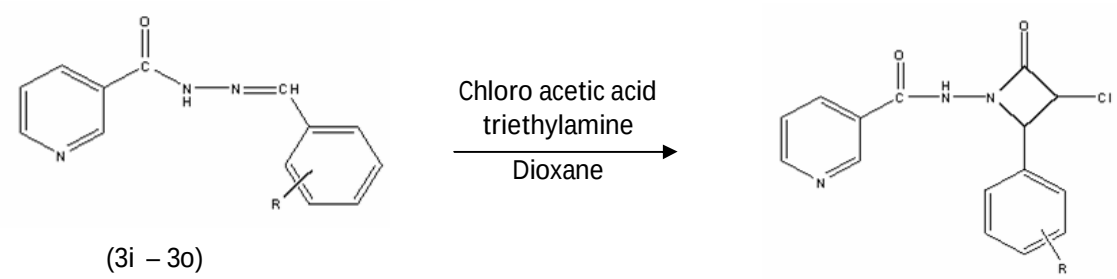
A new series of 4-Oxo-Azetidine derivatives **(4i-4o)** from Schiff bases are synthesized[8,9]. The Schiff base derivatives on treatment with dioxane and triethylamine afforded targeted compounds **(4i-4o)**. The structure of all synthesized compounds has been established on the basis of their spectral (IR, H^1&C^{13} NMR and Mass) and analytical data. The purity of the compounds was confirmed by TLC. All the synthesized compounds were evaluated for their antioxidant activity.

SCHEME

The list of synthesized compounds (4i– 4o).

4i) N- (3-chloro - 2(4^1-chloro phenyl) -4-oxo-azetidine-1-yl) nicotinamide.

Scheme:



(3i – 3o)

(4i – 4o)

Where R = p-chloro (4i), m-bromo(4j),o-chloro (4k),o-methoxy(4l),o,p-dimethoxy(4m),3^1,4^1,5^1 trimethoxy(4n), o-nitro (4o).

4j) N- (3-chloro -2 (3^1-bromo phenyl) -4-oxo-azetidine-1-yl) nicotinamide

4k) N- (3-chloro -2 (2^1-chloro phenyl) -4-oxo-azetidine-1-yl) nicotinamide

4l) N- (3-chloro -2 (2^1-methoxy phenyl) -4-oxo-azetidine-1-yl) nicotinamide

4m) N- (3-chloro -2 (2^1, 4^1 - dimethoxy phenyl) -4-oxo-azetidine-1-yl) nicotinamide

4n) N- (3-chloro -2 (3^1, 4^1, 5^1 - trimethoxy phenyl) -4-oxo-azetidine-1-yl) nicotinamide

4o) N- (3-chloro -2 (2^1-nitro phenyl) -4-oxo-azetidine-1-yl) nicotinamide

Where R = p-chloro (4i), m-bromo(4j),o-chloro (4k),o-methoxy(4l),o,p-dimethoxy(4m),3^1,4^1,5^1 trimethoxy(4n), o-nitro (4o).

Antioxidant Activity [10-13]:

All the synthesized compounds (4i-4o) were tested for their in vitro free radical scavenging Nitric oxide (NO) and scavenging of Superoxide radical with the alkaline DMSO method.

Assay of nitric oxide radical scavenging activity[14]:

Nitricoxide radical scavenging activity was assayed by using Griess reagent. The reaction mixture contained 5 ml of sample solution and ascorbic acid (standard) of different concentrations (25-200 µg / ml) in standard phosphate buffer solution (pH 7.4) , 5ml of sodium nitroprusside solution (5mM) in standard phosphate buffer (pH 7.4) and incubated for 5 hours at 25^{0}C.

Control was prepared without compound but with an equivalent amount of buffer. Then 0.5ml of the incubation mixture was mixed with 0.5 ml of Griess reagent (Sulphanilamide 1%, o-phosphoric acid 2% and naphthyl ethylene diamine dihydro chloride 0.1%) and the absorbance was measured at 546 nm against blank (DMSO). The experiments were performed in triplicate. From the absorbance the percent of scavenging activity was calculated as follows and the results were shown in **Table 1.**

Scavenging activity (%) =

$$\frac{[\,(A_{546}\ (\text{control}) - A_{546}\ (\text{sample})\,)]}{A_{546}\ (\text{control})} \times 100$$

Assay of Superoxide Radical Scavenging Activity[15]:

Superoxide radical scavenging activity was assayed by nitro blue tetrazolium system. The reaction mixture containing 0.1ml of nitro blue tetrazolium (1mg/ml in DMSO) and 0.3ml of synthesized compounds (4i-4o) or standard in DMSO was added (1ml of DMSO containing sodium hydroxide 5mM in 0.1 ml of water) to give a final volume of 1.4ml and the absorbance was measured at 560nm against blank (DMSO). The percentage scavenging of superoxide radical was calculated by using above formula. The results were shown in **Table 2.**

RESULTS AND DISCUSSION:

The nitric oxide assay has been widely used to evaluate the free radical scavenging effectiveness of various antioxidant substances.

Table 1: Nitric oxide Radical Scavenging activity for 4-oxo- Azetidine derivatives (4i-4o)

S.No	Conc. (µg/ml)	STD.	CTRL.	4i	4j	4k	4l	4m	4n	4o
1.	25	23.08	6.01	10.86	07.42	11.08	05.56	09.14	13.87	8.04
2.	50	34.64	6.01	21.67	07.44	20.86	16.76	15.89	19.67	11.95
3.	75	45.17	6.01	31.56	28.45	36.78	29.09	28.86	34.45	24.14
4.	100	59.29	6.01	49.97	37.98	48.91	38.66	41.14	49.97	30.86
5.	125	67.43	6.01	60.16	47.85	50.04	61.98	56.89	60.16	42.88
6.	150	79 .97	6.01	66.21	56.98	72.45	48.56	50.28	66.21	45.46
7.	175	87.76	6.01	77.98	69.87	84.32	76.69	62.86	77.98	56.86
8.	200	99.30	6.01	84.17	80.02	90.12	81.16	86.06	84.17	54.64

Table 2: Superoxide Radical Scavenging activity for4-oxo- Azetidine derivatives (4i-4o)

S.No	Conc. (µg/ml)	STD.	CTRL.	4i	4j	4k	4l	4m	4n	4o
1.	25	23.08	6.01	06.87	05.34	10.02	09.08	06.26	11.87	08.64
2.	50	34.64	6.01	11.67	15.43	27.86	18.08	19.65	21.67	14.95
3.	75	45.17	6.01	25.87	28.45	31.76	27.78	23.65	24.08	19.54
4.	100	59.29	6.01	49.97	37.98	48.91	31.67	27.76	49.97	30.86
5.	125	67.43	6.01	60.16	47.85	60.04	37.56	32.65	60.16	42.88
6.	150	79 .97	6.01	66.21	56.98	72.45	42.09	38.09	66.21	45.46
7.	175	87.76	6.01	77.98	69.87	84.32	46.86	43.65	77.98	56.86
8.	200	99.3	6.01	84.17	80.02	90.12	50.09	48.76	84.17	54.64

Nitric oxide generated as a result of decomposition of sodium nitroprusside in aqueous medium, interacts with oxygen at physiological pH to produce nitrite ions, which are measured by using Griess reagent. The nitrite ions were subjected to diazotization followed by azo coupling reaction to yield an azo dye, measured by an absorption band at 546nm. The scavenging ability of the synthesized compounds was compared with ascorbic acid as a standard. Compounds **4k &4m** produced better scavenging ability (**Table-1**). Compounds **4i, 4j, 4l** and **4m** showed moderate radical scavenging activity and **4o** compound showed least activity when compared to standard.

Even though superoxide radical is a weak oxidant, it gives rise to the generation of powerful and dangerous hydroxyl radical along with single oxygen , both of them lead to oxidative stress.

The experimental results suggest that **4k** showed better scavenging activity whereas **4i, 4j & 4n** exhibited moderate activity. Least activity is identified for the compounds **4l, 4m & 4o**.

CONCLUSIONS

4-Oxo- Azetidines exhibited significant to moderate activity when compared with standard ascorbic acid. Strong antioxidant activity was observed for N- (3-chloro -2 (2^1-chloro phenyl) -4-oxo-azetidine-1-yl) nicotinamide (**4k**) in both methods. The antioxidant capacity of the compounds were found to be 8.02 to 90.12 for different concentrations (25-200 µg/ ml).

REFERENCES

1. Ghulam Fareed and Nighat Afza , "reported antioxidant activity and structure activity relationship of some new Schiff bases derived from 2-amino benzo phenone", Medicinal chemistry and drug discovery; 4(1), 27-34, 2013.
2. Maaroof Zareia, Zahed Karimi-Jaberi and Amin Movahedi, "Synthesis of β-lactams from acids and imines using thiocarbonyl diimidazole", An International Journal for Rapid Communication of Synthetic Organic Chemistry ; 43(5), 2013.
3. V Gustavo P. Romanelli and Juan C. Autino, "recent applications of hetero polyacids and related compounds in heterocyclic synthesis", Mini-Reviews in Organic Chemistry; 6, 359-366, 2009.
4. Ravindra Kumar, Abha Shukla and D.S.Tyagi, "An efficient synthesis of bio active Azetidinones and thiazolidinones of 3-methyl-1-phenyl-1H-pyrazol-5-ol", International Journal of Scientific and Research Publications; 2(6), 2012.
5. Saudane AR, Rudresh K, Satyanarayana ND and Hiremath SP, Indian J Pharm Sci; 60, 379, 1998.
6. Raga Basawaraj, Amith L and VijayKumar T, Int J ChemTech Res ; 2(3),1764-1770,2010.
7. Jaishree vaijanthappa and shrishaillappa badami "Invitro antioxidant activity of enicostemma axillare", Journal of Health sciences; 54 (5), 524-528, 2008.
8. Praveen kumar P and B.L.Rani , " Synthesis and characterization of new Schiff bases containing pyridine moiety and their derivatives as antioxidant activity", Int J Chem Tech Res ; 4(3), 155-160,2011.
9. N.Madhavi and B.L.Rani "Synthesis of some new 4-oxo-Azetidine derivatives from Schiff base derivatives containing pyridine moiety as antimicrobial agents" , Int. J. Pharm Bio .Sci. ; 4(4) (B) , 951 -957, 2013.
10. M. A. Babizhayev, A. I. Deyev, V. N. Yermakova, I. V. Brikman, and J. Bours, "Lipid peroxidation and cataracts: N-acetyl carnosine as a therapeutic tool to manage age-related cataracts in human and in canine eyes", Drugs in R and D; 5(3), 125–139, 2004.
11. M. S. Cooke, M. D. Evans, M. Dizdaroglu, and J. Lunec, "Oxidative DNA damage: mechanisms, mutation and disease," FASEB Journal; 17(10), 1195–1214, 2003.
12. S. P. Hussain, L. J. Hofseth, and C. C. Harris, "Radical causes of cancer", Nature Reviews Cancer; 3(4), 276–285, 2003.
13. S. Suzen, Bozkaya, T. Coban, and D. Nebioglu, "Investigation of the in vitro antioxidant behaviour of some 2-phenylindole derivatives: discussion on possible antioxidant mechanisms and comparison with melatonin", Journal of Enzyme Inhibition and Medicinal Chemistry; 21(4), 405–411, 2006.
14. You-Zhi Tang and Zai-Qunlin, " reported structure activity relationship of hydroxyl substituent Schiff bases in radical induced heamolysis of human erythrocytes", Cell bio chemistry and function; 26(2), 185-191 ,2008.
15. Kumar A., Rout S., Sahoo D.K., Kumar B.V.V.R., "Synthesis and biological evaluation of new 4-bromo-3, 5-diaryl-1-phenyl-2-pyrazoline derivatives as antioxidant and anti-inflammatory agents", Int. J. Res. Dev. Pharm. L. Sci., 2012, 2 (2), pp. 349-354.
16. Zhao F and Liu ZQ," reported Indole and its alkyl-substituted derivatives protect erythrocyte and DNA against radical-induced oxidation", J Bio chem Mol Toxicol; 23(4), 273-279, 2009.

How to cite your article:
Madhavi N., Rani B.L.., "Antioxidant activity of novel 4-oxo-azetidine derivatives synthesized from schiff bases", Int. J. Res. Dev. Pharm. L. Sci., 2014, 3(2), pp. 905-908.

