Available Online through
www.ijpbs.com

IJPBS |Volume 2| Issue 2 |APRIL-JUNE |2012|143-149

SYNTHESIS AND CHARACTERIZATION OF NOVEL BENZIMIDAZOLE DERIVATIVES

B.Sri divya , K.Ramesh, N.Poornima*

Department of pharmaceutics, Sri Indu Institute of Pharmacy, Hyderabad, India.
***Corresponding Author Email:** sampath.surya76@gmail.com

PHARMACEUTICAL SCIENCES
RECEIVED ON 14-05-2012

RESEARCH ARTICLE
ACCEPTED ON 31-05-2012

ABSTRACT

Benzimidazoles and its derivatives represent one of the most biological active class of literature. The synthesized benzimidazole compounds were prepared from the condensation reaction between ortho phenylene diamine and various aromatic acids,in the presence of hydrochloric acid. The purity of the compounds was ascertained by melting point and thin layer chromatography. The synthesized compounds were characterized by using infrared spectroscopy. Benzimidazoles are known for their many therapeutic applications. It can be used in the conditions of inflammation, anxiety and microbial infections.

KEYWORDS: *Benzimidazoles, thin layer chromatography, phenylene diamine.*

INTRODUCTION

Medicinal chemistry is a science having its roots in all branches of chemistry and biology. It involves isolation, characterization and synthesis of new comounds that can be used as medicines for prohylaxis and curing of diseases. Medicinal chemistry thus from the chemical basis of therapeutics. The focus on development of new synthetic drug compounds resulted in the incorporation of many other discipline such as biochemistry and molecular biology into medicinal chemistry. There is a lot of collaboration between chemists and biologists while searching for a lead on a new drug or doing research on a pre-clinical drug candidate. The other areas of collaboration include biology, Computer aided drug design (CAD), X-ray crystallography. Together this team used sophisticated analytical techniques to synthesize and means of production. Following the discovery of benzimidazole derivatives have been structural modifications have been made to the benzimidazoles nucleus to increase the anti-inflammatory activity. Mannich bases of benzimidazoles were synthesized using different secondary amines. The h boiling formation of the products was confirmed by the analytical and spectral data. The benzimidazoles are high melting and high boiling solids. The parent compound melts at 170^0C. they are soluble in non-polar solvents. The pseudo benzimidazole and many of acidic character of its derivatives is reflected in the ability to form salts with metals.The ability to react with Grigard reagents to give the acidic nature of the benzimidazole and 2-substitution of the imino hydrogen eliminates the pseudoacidic character. A number of the addition of the appropriate metal amide to a solution of benzimidazole in liquid ammonia. These salts hydrolyze upon exposure to water the regeneration of benzimidazoles.Electronegative groups increase the acidic nature of the benzimidazoles. The nitrobenzimidazoles are strong enough acids to dissolve in sodium carbonate of ammonia. 2-methyl-4,6 (or) 5,7-dinitro benzimidazole forms a stable ammonia salt.

BASIC STRENGTH AND ELECTRONIC STRUCTURE

The benzimidazoles are predominantly basic compounds having the ability to form salts with acids. Benzimidazole (pKa 5.5) is a basic considerably weaker than the imidazole(pka 7.0). this difference in the basic strength is a reflection of the conjugation between the imidazole and benzene rings. Conjugation

increases the number of contributing states in the resonance structures. A to G represent the major contributions to the state of benzimidazole system. Structures D,E and G deicts the conjugation between the imidazoleand benzene portions which may be responsible for the difference in basic strength between imidazole and benzimidazoles. Symmetry consideration may offer a lausible explanation explanation for the observation that a methyl grou in the 1 position fails to increase the basic strength of benzimidazole.

REVIEW OF LITERATURE

Salgoankar P.D et al., reported the synthesis of substituted amino analogs of 2-(a-hydroxy benzyl). Benzimidazoles from o-phenylene diamine with Mandelic acid. The synthesized cond exhibited compound exhibited significant of microbiological activity.

R.N Goyal et al., reported the synthesis of 2-amino benzimidazole at pyrolytic graphite

V.K.Pandey et al., reported by the synthesis of 2-substituted benzimidazole. This compounds exhibit antiviral activity.

Sarhan et al., reported the synthesis of substituted 4-hydrazino-2-methylpyrimidino[4',5':4,5]thiazole [3,2-a]benzimidazole.

Mashooda Hassan et al., reported the synthesis of 5-Nitro benzimidazole. The synthesized compound exhibited by the significant anti-inflammatory and anti-viral activity.

S.Shawkat naim et al., reported the synthesis of substituted 2-alkyl/aryl-carbonylamino benzimidazole. This synthesised compound exhibit anti-helminthic activity and antiparasitic activity.

Prithpal singh et al., reported the synthesis of 2-substituted benzimidazole from o-phenylene diamine with arylalkanoic acid. The synthesised compound was exhibited significant anti-inflammatory activity at 100mg/kg and it possesses antifungal activity against Aspergillus niger.

Mehboob et al., reported the synthesis and anti-inflammatory activity of benzimidazolo (2,3-a) phthalazines. The synthesized compounds exhibited anti-inflammatory and anti-hypertensive activity.

Rashmi rastogi et al., reported the synthesis of benzimidazzole 2-carboxides and screened for anti-helminthic activity. The synthesized compound did not posses significant against nipostrongylus brascillenisis in rats and nematospiroides dubis in mice.

Joel R. Huff et al., reorted the synthesis of substituted 2,3,4,5-tetrahydro

A Narayan reddy et al., reported the synthesis of substituted imidazolino-[3,4-a]-2,3-a]-dihydro imidazoles/benzimidazoles. The synthesised compounds exhibited significant of anti-inflammatory activity.

P.K.Dubey et al., reported the synthesis of 1-substituted-2-α-bromoacetyl benzimidazoles with oxygen nucleophiles. The synthesised compound exhibited the biological activity.

MATERIALS AND METHOD

1. SCOPE OF THE EXPERIMENT

Chemical modifications of drug molecule of a series having optimum activity is widely used and continue to be an important factor in new drug discovery studies. In order to obtain new, effective and safe drugs has led today's researches to improve existing drugs by increasing their potency, duration of action by decreasing their toxic side effects. Structural activity studies show that variations in ring system as minor group extend distinct pharmacological effect upon the drug molecules. The ring system in which a benzene ring was fused to an imidazole ring at 4,5 positions is called as benzimidazole. Benzimidazole was prepared by reacting o-phenyldiamine with any carboxylic acid. The present experiment was carried out by using different carboxylic acids. Benzimidazoles show anti inflammatory activity. The present work is carried to synthesize benzimidazoles using different carboxylic acids to achieve better anti inflammatory properties.

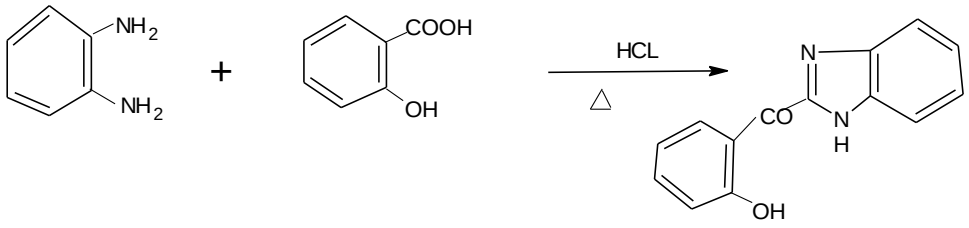
2. SCHEME OF THE EXPERIMENT

Ortho phenylene diamine(OPDA) was condensed using different carboxylic acids in the presence of HCl to give benzimidazoles using different carboxylic acids is depicted below:

GENERAL REACTION

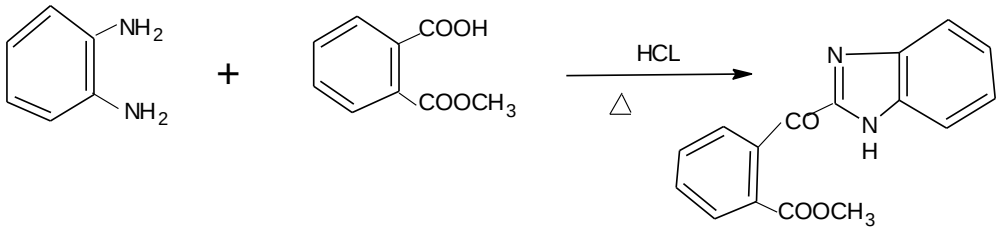
O-Phenylene diamine + COOH-R ⟶ Benzimidazole

(a) OPDA + salicylic acid = benzimidazole



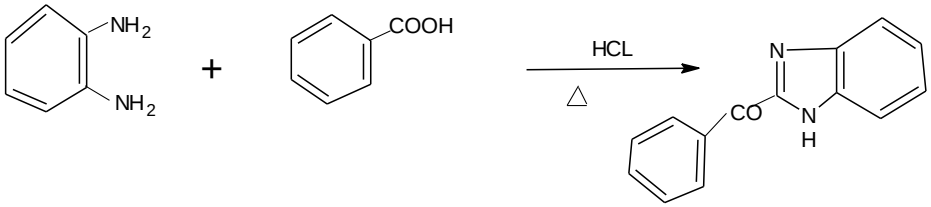
(Compound 1)

(b) OPDA + acetyl salicylic acid = benzimidazole



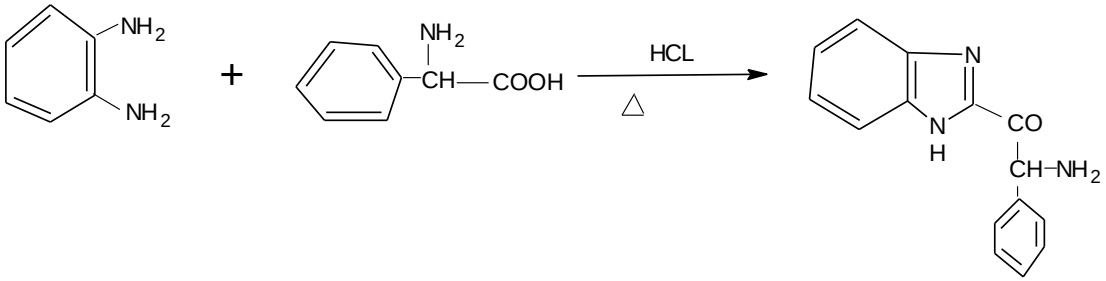
(compound 2)

(c) OPDA + benzoic acid = benzimidazole



(Compound 3)

(d) OPDA + phenyl glycine = benzimidazole



(Compound 4)

PROCEDURE

1. CHEMICALS:

Ortho phenyl diamine
Hydrochloric acid
Phenyl glycine
Salicylic acid
Acetyl salicylic acid
Benzoic acid

2. PREPARATION OF REAGENTS:

(A) Preparation of 4N HCl: 36.5gms of HCl = 1000ml water ; 14.6gms of HCl = 100ml water

100ml of 4N HCl was prepared by dissolving 14.6gms of HCl in 100ml of distilled water.

(B) Preparation of TLC reagent:

For the identification of benzimidazoles using thin layer chromatographic technique the reagent used is a mixture of ethyl acetate, n-hexane and methanol taken in a ratio of 3:2:1.

EXPERIMENT

(A) REACTION OF OPDA WITH SALIVYLIC ACID:

Benzimidazole was synthesized by o-phenylene diamine(12mmol) and salicylic acid(36mmol) in the presence of 4N HCl(40ml) and refluxed for 4hrs, then cooled at room temperature. The percentage yield of the compound was found to be 81%.

(B) REACTION OF OPDA WITH ACETYL SALICYLIC ACID:

Benzimidazole was synthesized by o-phenylene diamine(12mmol) and acetyl salicylic th room temperature. The percentage yield of the compound was found to be 81.4%.

(C) REACTION OF OPDA WITH BENZOIC ACID:

Benzimidazole was synthesized by 0-phenylene diamine (12mmol) and benzoic acid (36mmol) in the presence of 4N HCl (40ml) and reluxed for 4hrs. Then cooled at room temperature. The percentage yield of the compound was found to be 83%.

(D) REACTION OF OPDA WITH PHENYL GLYCINE:

Benzimidazole was synthesized by o-phenylene diamine (12mmol) and phenyl glycine (36mmol) in the presence of 4N HCl (40ml) and refluxed for 4hrs. Then cooled at room temperature. The percentage yield of the compound was found to be 82%.

RESULTS AND DISCUSSION

LIST OF MELTING POINTS, RETARDATION FACTORS AND PERCENTAGE PURITIES OF THE SYNTHESIZED COMPOUNDS:

S.NO	COMPOUND	MELTING POINT	RETARDATION FACTOR	PERCENTAGE YEILD
1	COMPOUND 1	179^0 C	1.9	81%
2	COMPOUND 2	179^0 C	1.7	81.2%
3	COMPOUND 3	178.2^0 C	1.8	83%
4	COMPOUND 4	178^0 C	1.8	82%

IR RANGES:

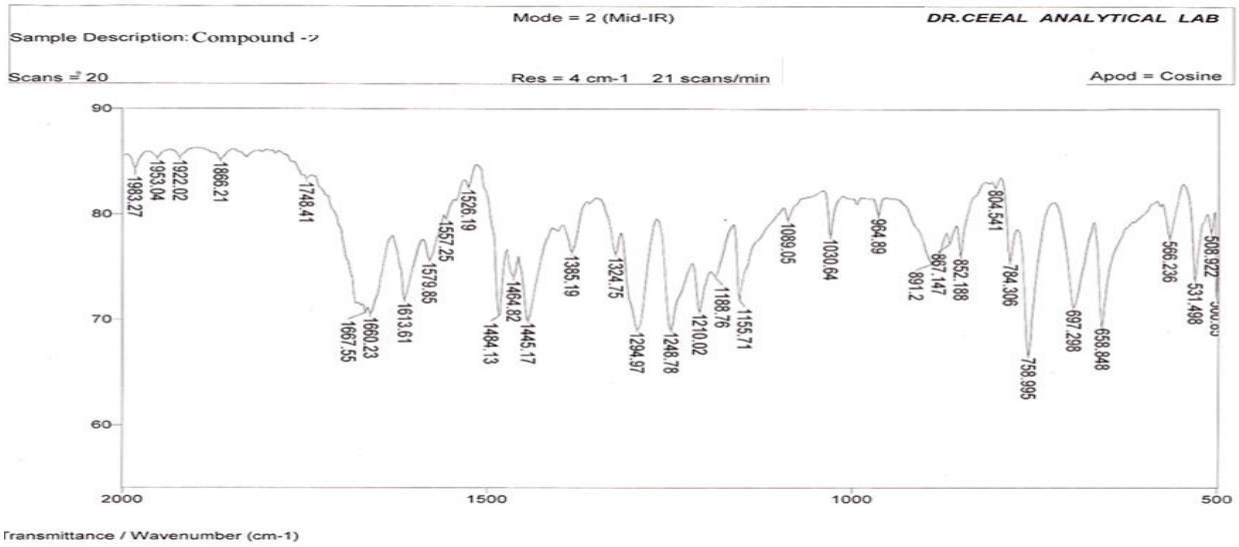
Infrared spectral λ_{max} cm^{-1} assessment data of the synthesized Compounds are shown below.

S.No	Compounds	C= N	C=C	Ar	NH
1	1	$1661_{(w)}$	$1581_{(m)}$	$774_{(w)}$	$1387_{(m)}$
2	2	$1658_{(m)}$	$1578_{(m)}$	$758_{(s)}$	$1325_{(m)}$
3	3	$1683_{(w)}$	$1581_{(s)}$	$795_{(s)}$	$1316_{(s)}$
4	4	$1660_{(m)}$	$1579_{(m)}$	$784_{(s)}$	$1324_{(m)}$

IR FIGURES:

OPDA was condensed with salicylic acid and in presence of HCL and the completion of the reaction was confirmed by TLC and characterized by IR spectroscopy.

Compound 1 (salicylic acid):



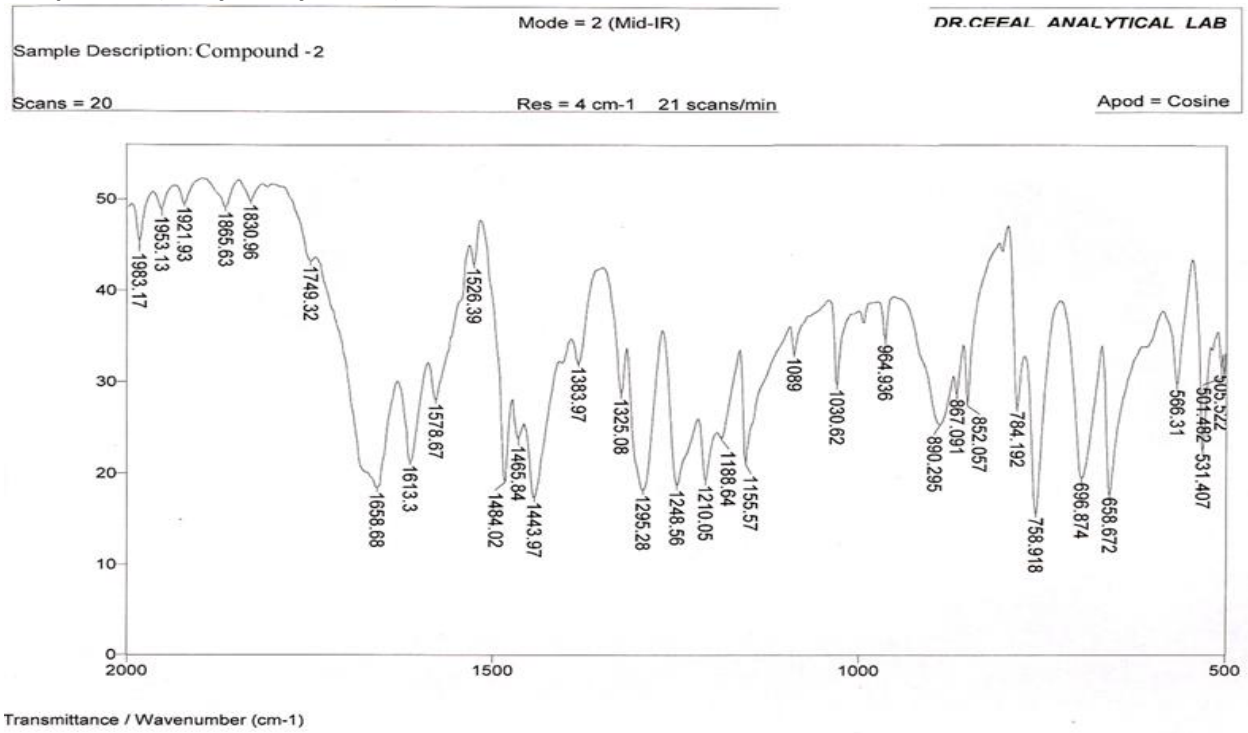
Melting point – 179^{o}C

Retardation factor – 1.9

Percentage yield – 81%

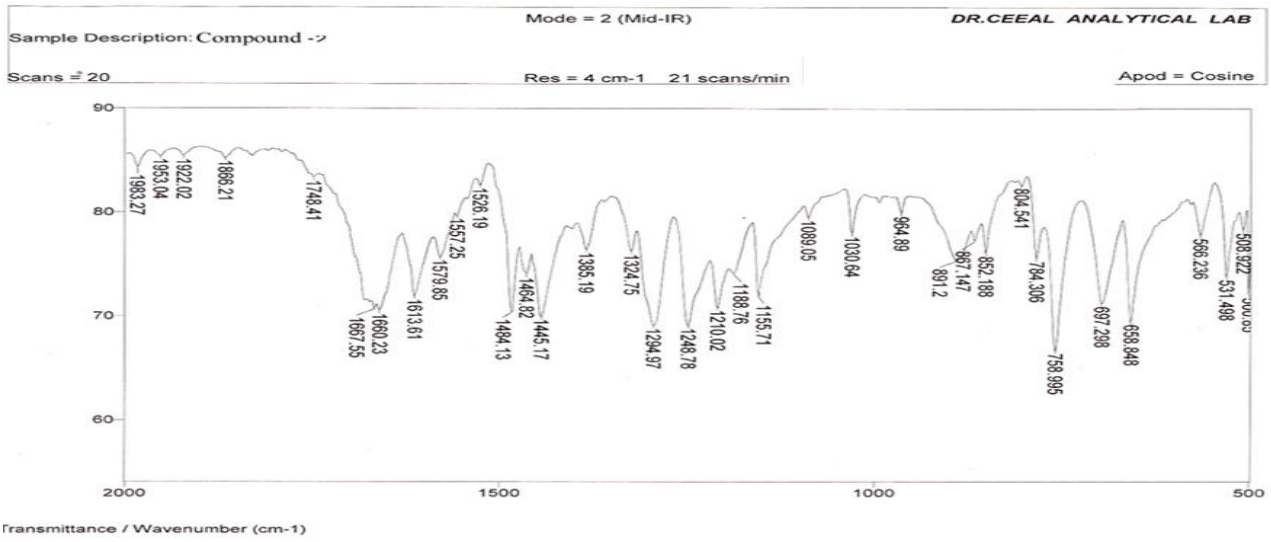
OPDA was condensed with acetyl salicylic acid in the presence of HCl and the completion of the reaction was confirmed by TLC and was characterized by IR spectroscopy.

Compound 2(acetyl salicylic acid):



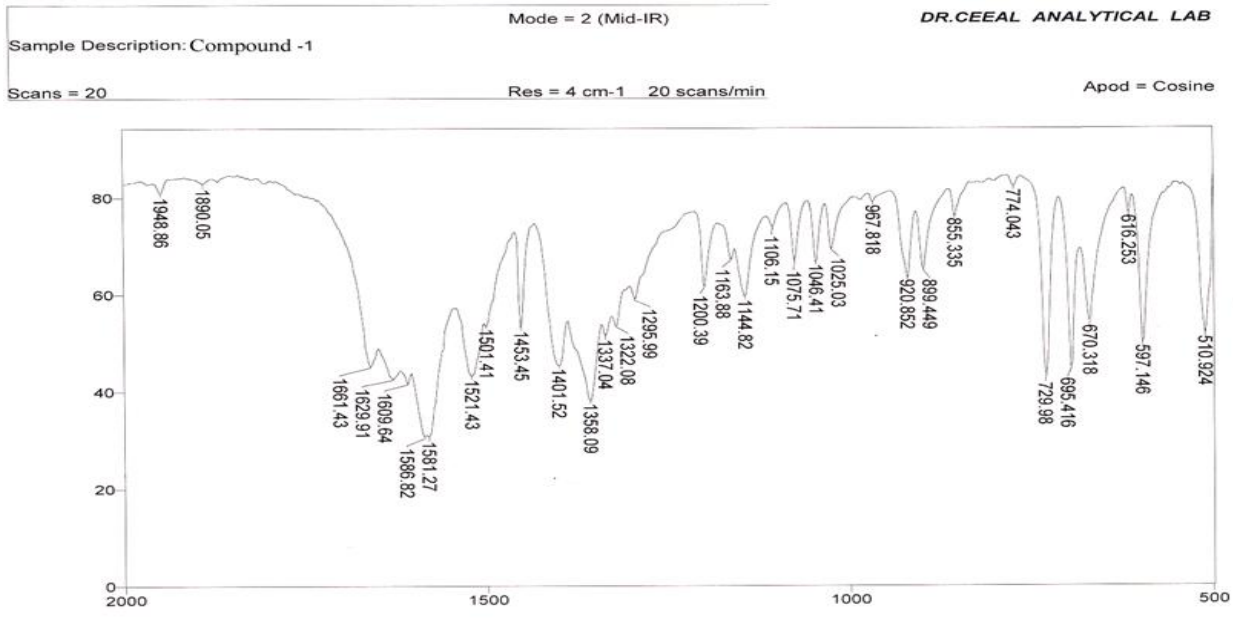
Melting point – 179°C
Retardation factor – 1.7
Percentage yield – 81.2%
OPDA was condensed with benzoic acid in the presence of HCl and the completion of the reaction was confirmed by TLC and was characterized by IR spectroscopy.

Compound 3(benzoic acid):



Melting point – 178.2°C
Retardation factor – 1.8
Percentage yield – 83%
OPDA was condensed with phenyl glycine in the presence of HCL and the completion of the reaction was confirmed by TLC and was characterized by IR spectroscopy.

Compound 4(phenyl glycine):



Melting point – 178°C
Retardation factor – 1.6

Percentage yield – 82%

CONCLUSION

In the present work, ortho phenylene diamine (OPDA) which was condensed with different acids such as phenyl glycine, salicylic acid, acetyl salicylic acid and phenyl acetic acid. The completion of the reaction was confirmed by TLC and was characterized by IR. The melting point of the synthesized compounds was measured by using open capillary tube method.

REFERENCES:

1. Salgaonkar P .D and Velingkar V.S , Indian drugs , VOl . 37(11) , Nov 2000 PP 547 – 550.
2. R . N . Goyal and Amit K Srivastava , Indian journal of chemistry, Vol . 31 A , 1992 , PP 794 – 796.3
3. V . K . Pandey , K . C . Khulbe , G . Saxena , P . Gupta and K . Chendra , Indian drugs , Vol . 21, 1984 , PP 135 – 138.
4. Sarhan , Hozien , Mahmoud ,Journal of Chinese chemical society , Vol .47 , 2000 , PP 1279 – 1286.
5. M . A . Raslam , M . A . Selim , Journal of Chinese chemical society , Vol . 47 , 2000 , PP 961 – 965.
6. Murali Manohar Tiwari , V . K .Saxena , S . K .Balaji , A . J . Srivastava, M . N . Joshi, Indian drugs ,Vol . 30(7) , PP 327 – 330.
7. S . John winston , P . Jayaprakash Rao , B . Sethuram , T . Navaneeth Rao , Indian Journal of chemistry , VOl . 28 A , 1989 , PP 520 – 522
8. Magdum chandrakanth . S , Shirodkar P . Y and Paannikar K . R , Indian drugs , VOl . 37(11) , 2000 , PP 528 – 532.
9. Andi C Dash , Achutananda Acharya , Ranaa K Sahoo , Indian Journal of chemistry , VOl . 37A , 1998 , PP 759 – 764.
10. Mashooda Hasan , Journal of chemistry , Vol . 24 , 2000 , PP 73 – 79.
11. V . K . Pandey , Naveen Raj , U . K . Srivastava , Indian drugs , Vol.23(11) , 1986 , PP
12. K . L . Omprakash , A . V . Chandrapal , M . L . N . Reddy , Indian Journal of chemistry , Vol . 21 A , 1987 , PP 322 – 323.
13. S .Shawkat Naim , Sudhir K Singh and Satyavan Sharma , Suman Gupta , A . M . Khan , K . K . Chetterjce , J . C . Katiyar , Indian journal of chemistry , VOl . 29 B , 1990 , PP 464 – 470.
14. G . H . Gavanur , V . K . Revankar , K . V . B . Mahale , Indian Journal of chemistry , Vol . 30A , 1991 , PP 474 – 476.
15. Pritpal Sing and LL Hingorani., Indian Journal of Chemistry, 1990, Vol . 29B, 596 – 597.
16. Singh. S.P, Omprakash, R.K. Tomer and SN. Sawhney., Indian, J. Chem 1978, Vol . 16B, 733 – 735.
17. Mehboob Razvi and T. Ramalingam., Indian Journal of Chemistry., 1992, 313, 788 – 789.
18. Rashmi Rastogi, Stayavan Sharma, and RN Iyer., Indian J.chemistry, 1979, Vol . 18B, 464 –4 67.
19. Syed Abuzar, Satyavan Sharma and RN Iyer., Indian J. Chemistry, 1980, Vol . 19B, 599 – 600.
20. Agarwal.V.K, Stayavan Sharma, R.N. Iyer., Indian J. Chemistry, 1981, Vol . 20B, 398 – 400.
21. Sudhir .k Singh, S. Shawkat Naim and Satyavan Sharma, Suman Gupta and J.C. Katiyar., Indian Journal of Chemistry, 1989, 28B, 397402.
22. Sawhney.S.N, Dharamvir and Pradeepkumar., Indian Journal of Chemistry, 1989, Vol . 28B, 574 – 578.
23. Alka Agarwal, Shiv K. Agarwal and D.S. Bhakuni Somnath Singh and R.K. Chatterjee., Indian Journal of Chemistry., 1993,Vol . 32B, 453 – 456.
24. Ravi P. Srivastava, Sudhir K. Singh, Syed Abuzar, Satyavan Sharma Suman Gupta, J.C. Katiyar and R.K. Chatterjee., Indian J. Chemistry, 1993, Vol . 32B, 1035 – 1044.
25. Joel R. Huff, Stella W. King and Waltred S. Saari., J. Org. Chem,1982, Vol . 47, 582 –585.
26. A . Narayan Reddy , Sujata Patnaik , Navneeth Kalyane , V . M . Reddy Pratibha Sharma, Anupam Mandloi and Shreeya Pritmani., Indian.J. Chemistry, 1999, Vol . 38B, 1289 – 1294.
27. Jyothi R . Kavali and Barathi V . Badani ,Indian Journal Heterocyclic chemistry , Vol . 12 , 2003 , PP 249 – 252.
28. P . K . dubey , C . Ravikumar and P . V . V .Prasada Reddy , Indian Journal of Heterocyclic chemistry , Vol .12 , 2003 , PP 213 – 216.
29. Sukvinder Kaur Chawla , Indian Journal of chemistry , Vol . 37 A , 1998 , PP 904 – 907.
30. Lata Nohria , Manisha Gupta and Pavan Mathur , Indian Journal of chemistry , Vol . 37 , 2001 , PP247 – 251.
31. Abdou O Abdelhamid , Hussein F Zohdi and Mahmoud M Ziada , Indian Journal of chemistry , Vol . 39 B , PP 202 – 209.
32. P . Thakur , V . Chekravorthy and K C Dash , Indian Journal of chemistry , Vol . 38 B , 1999 , PP 1223 – 1227.

***Corresponding Author:**
B.Sri divya
Department of pharmaceutics,
Sri Indu Institute of Pharmacy,
Hyderabad, India.