Ph. D. Thesis

SYNTHESIS AND PHYSICO CHEMICAL PROPERTIES OF SOME BIO ACTIVE HETEROCYCLIC ENTITIES

BY

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DEPARTMENT OF CHEMISTRY
(DST-FIST FUNDED & UGC-SAP SPONSORED)
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BY

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UNDER THE GUIDANCE
OF

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Statement under O.Ph.D. 7 of Saurashtra University

The work included in the thesis is my own work under the supervision of **Dr. Shipra Baluja** and leads to some contribution in chemistry subsidized by a number of references.

Date: 1 -01-2010

Place: Rajkot **(Jagdish R. Movaliya)**

This is to certify that the present work submitted for the Ph.D. Degree of Saurashtra University by **Jagdish R. Movaliya** is his own work and leads to advancement in the knowledge of chemistry.

The thesis has been prepared under my supervision.

Date: 1 -01-2010

Place: Rajkot.

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Dedicated To My Family

&

Beloved Guide

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Mr. Rameshbhai V. Movaliya *and* ***Mrs. Manjulaben R. Movaliya*** *for their untiring support in the form of love during the period of my study. Also my sincere gratitude towards many more well-wishers, friends and relatives who directly or indirectly rendered me valuable help and moral strength during this work.*

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Jagdish R. Movaliya

CONTENTS

SYNOPSIS

SYNTHESIS AND PHYSICO CHEMICAL PROPERTIES OF SOME BIO ACTIVE HETEROCYCLIC ENTITIES

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SYNOPSIS of the thesis to be submitted to the Saurashtra University for the degree of **Doctor of Philosophy** in Chemistry.

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Compounds classified as heterocyclic probably constitute the largest and most varied family of organic compounds. These compounds show vital role in the field of pharmaceuticals because of their specific clinical reactivity, eg. epoxides, aziridines and β-lactams. The introduction of heterocyclic group into drugs may affect their physical properties, for example the dissociation constants of sulpha drugs or modify their patterns of absorption, metabolism, toxicity etc.

Taking in view of the applicability of heterocyclic compounds, the present work was undertaken to synthesize some new heterocycles bearing chloro quinoline nucleus. All the synthesized compounds were characterized by IR, NMR and mass spectra. Further, physicochemical properties such as acoustical properties, density, refractive index, conductance, heat of solutions, partition coefficient, thermal properties and dissociation constants of some compounds have also been studied in different solvents. The antibacterial activity of these compounds has also been studied.

The present work is divided into four chapters.

Chapter-1 General Introduction

Chapter-2 Synthesis and characterization

Part-1 Synthesis and characterization of Chloro Quinoline Derivatives

Section-I Cyanopyridines

Section-II Aminopyrimidines

Section-III 1, 5- Benzodiazepines

Section-IV Pyrazolines

Section-V Sulphonamides

Part-2 Comparison of different methods of synthesis

Chapter-3 Physico chemical properties

Section-I Acoustical Properties

Section-II Density and Refractive index

Section-III Conductance

Section-IV Heat of Solutions

Section-V Partition Coefficient

Section-VI Thermal Properties

Section-VII Dissociation Constants

Chapter-4 Biological activities

CHAPTER – 1: GENERAL INTRODUCTION

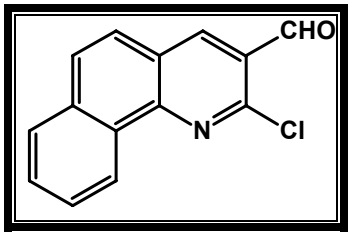
This chapter describes literature survey of synthesis, characterization, applications, physicochemical properties and antibacterial activities of heterocyclic compounds.

CHAPTER – 2: SYNTHESIS AND CHARACTERIZATION

This chapter deals with synthesis and characterization of some quinoline derivatives.

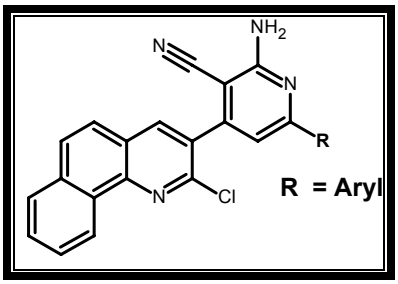
PART – 1: SYNTHESIS OF CHLORO QUINOLINE DERIVATIVES

The compounds containing chloro quinoline ring system have been of great interest to synthetic and medicinal chemist for a long time due to the unique chemical and biological properties imparted by hetero atom because of their utilization as effective biologically active agent like antimalarial, antiviral, analgesic, antitumor etc. Quinoline contains a phenyl ring fused to a pyridine ring.

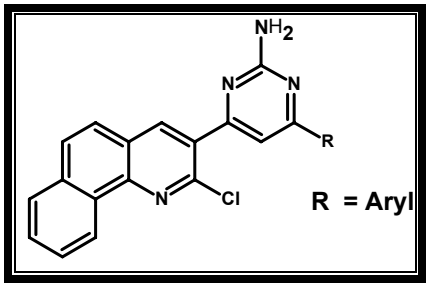


Thus, the important role displayed by quinoline and its derivatives for various therapeutic and biological activities prompted us to synthesize following derivatives:

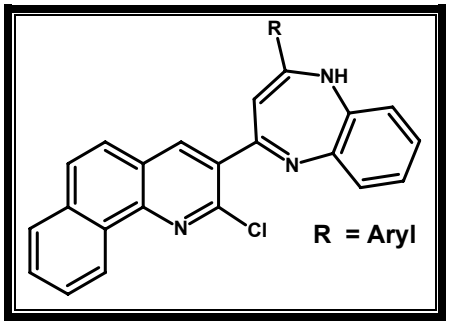
Section-I Cyanopyridines



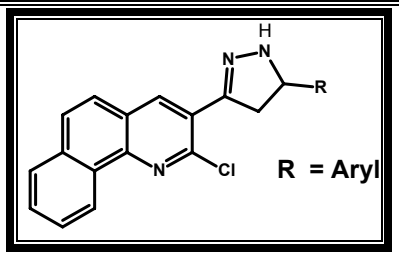
Section-II Aminopyrimidines



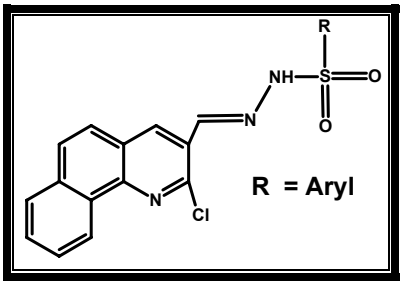
Section-III 1,5-benzodiazepines



Section-IV Pyrazolines



Section-V Sulphonamides



PART – 2: COMPARISON OF DIFFERENT METHODS OF SYNTHESIS

In this part, pyrazoline derivatives have been synthesized by microwave, ultrasound irradiation and conventional methods. The % yield and reaction time of these methods are compared.

CHAPTER – 3: PHYSICO-CHEMICAL PROPERTIES

Some physicochemical properties of cyanopyridine derivatives have also been studied in dimethylformamide and dimethyl sulphoxide. The various physico chemical properties are discussed in the following seven sections:

Section-1 Acoustical Properties

Acoustical properties of cyanopyridine derivatives in dimethylformamide and dimethyl sulphoxide were studied by measuring density, viscosity and sound velocity (at 2 MHz) at 298.15 K. From these experimental data, various acoustical parameters such as isentropic compressibility, Rao's molar sound function, specific acoustical impedance, internal pressure, Vander Waals constant, solvation number etc. were

evaluated and the results are discussed in the light of solvent – solute and solute – solute interactions.

Section-2 Density and Refractive index

Refractive index is a property of the material and is extremely useful in chemical analysis. Further, molar refraction is of great importance for the calculation of dipole moment. In this section, the density and refractive index of cyanopyridine derivatives were measured in dimethylformamide and dimethyl sulphoxide solutions at 298.15 K.

From the refractive index measurements, the density and refractive index of studied compounds were determined.

Section-3 Conductance

This section deals with the conductance measurement of solutions of cyanopyridine derivatives in dimethylformamide and dimethyl sulphoxide solutions over a wide range of concentration at 298.15 K. From these experimental values, equivalent conductance at infinite dilution for studied compounds was evaluated.

Section-4 Heat of Solutions

The molar heat of solution and melting temperature of a substance can be determined from the solubility measurement at different temperatures. In the present section, heat of solutions for cyanopyridine derivatives was determined at different temperatures (298.15-308.15 K) in dimethylformamide and dimethyl sulphoxide.

Section-5 Partition Coefficient

This section describes the partition coefficient of cyanopyridines in Water-
Octanol system by UV spectroscopy. From the spectral data, log P values were
evaluated.

Section-6 Thermal Properties

This section describes the thermal properties of cyanopyridine derivatives. The Thermo Gravimetric Analysis (TGA) and Differential Thermal Analysis (DSC) measurements were made. From these measurements, various kinetic parameters were evaluated. Further, thermal stability of various compounds were also determined.

Section-7 Dissociation Constants

This section deals with the dissociation constant of cyanopyridines in DMF-water system at 298.15 K.

CHAPTER – 4: BIOLOGICAL ACTIVITIES

In the present chapter, antibacterial activity of synthesized compounds was studied against some Gram positive and Gram negative bacteria in DMF and DMSO.

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GENERAL INTRODUCTION

Heterocyclic Chemistry has been progressing owing to their wide natural occurrence with specific chemical reactivity and broad spectrum utility. Heterocyclic compounds are those which have a cyclic structure with two or more different kinds of atoms in the ring. Carbon is still by far the most common ring in heterocyclic compounds and one or more of the carbon atom is replacement atom other than carbon usually nitrogen, oxygen, sulfur or other heteroatom.

Heterocyclic compounds play an important role in industry as well as in our life. Various natural products contain heterocyclic compounds such as alkaloids and glycosides and they have been used in medicinal since ancient time. Most of the alkaloids are nitrogenous bases, occurring in plants. Further, many antibiotics including penicillin and streptomycin also contain heterocyclic ring system. Many pigments such as indigo, hemoglobin and anthocynin are also heterocyclic compounds. Important drugs such as suphathiazol, pyrethrin, rotenine, cocaine, barbiturates also possess heterocyclic system. These compounds are also known to be used as starting material for the synthesis of new drugs[1-6].

Due to multiple utility of heterocyclic compounds in various fields mainly in pharmaceutics[7-11], pesticides[12-16], veterinary[17-19], dyes[20-23], polymers[24-26], automobiles[27-29] etc, various workers have synthesized these compounds.

Synthetic method for obtaining heterocyclic compound may be divided into ring closure reaction, addition reaction and replacement reaction.

Looking to the various applications of heterocyclic compounds[30-35], in the present work several heterocyclic entities have been designed, generated and were characterized using spectral studies. The study of some new heterocyclic compounds having benzoquinoline moiety have been selected for

the present work. The compounds containing benzoquinoline ring system have been of great interest to synthetic and medicinal chemists for a long time due to the unique chemical and biological properties.

AIMS AND OBJECTIVES:

The detail of the work done is as follows:

- To synthesize several derivatives like cyanopyridines, aminopyrimidines, benzodiazepines, pyrazolines and sulphonamides containing benzoquinoline moiety.
- To compare synthesis of benzoquinoline based pyrazolines using microwave, ultrasound induced and conventional thermal synthesis methods.
- To characterize these synthesized compounds for structure elucidation IR, ^{1}H NMR and Mass spectral studies.
- To study the physicochemical properties such as acoustical properties, density, refractive index, conductance, heat of solutions, partition co-efficient, thermal properties and dissociation constants of cyanopyridines, in different solvents.
- To evaluate antimicrobial activity of these synthesized compounds against some Gram positive, Gram negative bacterial strains as well as against fungal strain, in different solvents.

REFERENCES

[1] H. Matsubara, Y. Obara and N. Kuba; "Biological activity of heterocyclic compounds. II. Blindness in baby chicks caused by administration of guanamines, guanides, and their related compounds." *Nipp. Nog. Kag. Kaishi., 49, 505-11 (1975).*

[2] Y. Obara, Y. Umemoto and H. Matsubara; "Studies on the biological activity of heterocyclic compounds. Part IV. On the blinding activities and acute oral toxicities of aminobenzenes, pyrimidines, purines, amino-s-triazines and their related compounds in baby chicks." *Nipp. Nog. Kag. Kaishi.*, ***55***, *1205-12 (1981).*

[3] F. Saczewski and J. Saczewski; "Applications of 2-chloro-4, 5-dihydroimidazole in heterocyclic and medicinal chemistry." *Trend. Hetero. Chem.*, ***9***, *19-31 (2003).*

[4] J. B. Sperry and D. L. Wright; "Furans, thiophenes and related heterocycles in drug discovery." *Curr. Opini. Drug Disco. Develop.*, ***8***, *723-40 (2005).*

[5] M. Raposo and M. Manuela; "Recent developments in the chemistry of 2-thienylpyrroles: synthesis, reactivity and applications." *Targets in Hetero. Syst.*, ***11***, *122-54 (2007).*

[6] W. Su, W. Zhang, T. Wang and X. Yan, Cai, J. Duan; "Naphthane compound, derivative of Andrographolide and its medicinal application." *Fami. Zhu. Shen. Gong. Shu.*, 33, (2008).

[7] M. Winn, D. Arendsen, P. Dodge, A. Dren, D. Dunnigan, R. Hallas, K. Hwang, J. Kyncl, Y. Lee, N. Plotnikoff, P. Young and H. Zaugg; "Drugs derived from cannabinoids. 5. delta6a,10a-Tetrahydrocannabinol and heterocyclic analogs containing aromatic side chains." *J. med. Chem., **19(4)**, 461-71, (1976).*

[8] J. Renault, S. Giorgi, M. Baron, P. Mailliet, C. Paoletti, S. Cros and E. Voisin; "Heterocyclic Quinones. 4. A new highly cytotoxic drug: 6,7-bis(1-aziridinyl)-5,8-quinazolinedione." *J. med. Chem., **26(12)**, 1715-9, (1983)*

[9] C. Supuran, A. Scozzafava and J. Andrea; "Carbonic anhydrase inhibitors. Part 54. Metal complexes of heterocyclic sulfonamides: a new class of antiglaucoma agents." *Metal-Based Drugs, **4(6)**, 307-15, (1997).*

[10] P. Vicini, A. Geronikaki and M. Incerti; "Aminoderivatives of benzothiazole/benzoisothi -azole heterocycles as intermediates in the synthesis of novel therapeutic agents." Trudy Mezhdunarodnoi Konferentsii "Khimiya i Bio. Aktivnost Kislorod-i Serusoderz hashchikh Geterotsiklov"], *2nd, Moscow, **1**, 211-216 (2003).*

[11] J. Salvador, R. Pinto and S. Silvestre; "Recent advances of pharmaceutical interest." *Current Org. Syn., **6(4)**, 426-70 (2009).*

[12] G. Holan; Mode of action of DDT- new aryl-alicyclic and heterocyclic insecticides." *Environ. Qua. Safety, **3**, 359-64 (1975).*

[13] M. Johnston, J. Lohr, J. Moes, K. Solomon and E. Zaborski; "Toxicity of synergized and unsynergized nitromethylene heterocycle insecticide (SD 35651) to susceptible and resistant strains of Musca domestica." *J. eco. entomology, **79(6)**, 1439-42, (1986).*

[14] P. Stehrer and H. Wolf, "Genotoxic evaluation of three heterocyclic N-methylcarbamate pesticides using the mouse bone marrow micronucleus assay and the Saccharo myces cerevisiae strains D7 and D61.M." *Mutation res., **345(3-4)**, 111-25, (1995).*

[15] J. Samaritoni, D. Demeter, J. Gifford, G. Watson, B. Gerald, S. Margaret and J. Bruce; "Dihydropiperazine Neonicotinoid Compounds.Synthesis and Insecticidal Activity." *J. Agricul. Food Chem., **51(10)**, 3035-42 (2003).*

[16] Y. Liu, E. Zhao, W. Zhu, H. Gao and Z. Zhou; "Determination of four heterocyclic insecticides by ionic liquid dispersive liquid-liquid microextraction in water samples." *J. chromatography A, **1216(6)**, 885-91(2009).*

[17] H. Zhang and C. Huang; "Reactivity and transformation of antibacterial N-oxides in the presence of manganese oxide." *Environ. Sci. tech., **39(2)**, 593-601, (2005).*

[18] S. Oh, J. Park, M. Lee, S. Park, H. Jong and K. Choi; "Ecological hazard assessment of major veterinary benzimidazoles: acute and chronic toxicities to aquatic microbes and invertebrates." *Environ. Toxicolo. Chem., **25(8)**, 2221-26, (2006).*

[19] V. Furtula, L. Huang and P. Chambers; "Determination of veterinary pharmaceuticals in poultry litter and soil by methanol extraction and liquid chromatography-tandem mass spectrometry." *J. Environ. Sci. Health, **44(7)**, 717-23, (2009).*

[20] G. Boffa, C. Paffoni and N. Mazzaferro; "New heterocyclic vat dyes." *Annali di Chim. **64(11-12)**, 825-31, (1974).*

[21] R. Raue, H. Harnisch and K. Drexhage; "Dyestuff lasers and light collectors- two new fields of application for fluorescent heterocyclic compounds." *Heterocycles, **21(1)**, 167-90, (1984).*

[22] A. Towns; "Developments in azo disperse dyes derived from heterocyclic diazo components." *Dyes and Pigments, **42(1)**, 3-28, (1999).*

[23] M. Dekhtyar; "Approximation of basicity and absorption region in large arrays of polymethine dyes with heterocyclic end groups." *Dyes and Pigments, **74(3)**, 744-48, (2007).*

[24] W. Gibbs; "Synthesis of certain aromatic heterocyclic polymers." *J. Macromole. Sci. Chem., **2(7)**, 1291-1302, (1968).*

[25] W. Waddell and U. Younes; "Radiative stability of the heterocyclic polymer BBB." *J. Poly. Sci. Poly. Phy., **18(4)**,891-6, (1980).*

[26] F. Lu; "Preparation and functional properties of heterocyclic and aromatic polymers." *Cur. Trends in Poly. Sci., **4**, 263-71, (1999).*

[27] W. Schneider; "Two-component epoxy resin/amine systems as raw materials for high-solid coatings." *High Solids Coatings, **8(4)**, 3-17, (1983).*

[28] E.Enami and Y. Tamano; "Antistatic and weather-resistant propylene polymer compositions." *Jpn. Kokai Tokkyo Koho, 7, (1998).*

[29] H. Harashina; "Fire-resistant resin compositions, their manufacture, and their oldings with suppressed mold deposition and bleed out of fireproofing agents." *Jpn. Kokai Tokkyo Koho, 54, (2004).*

[30] U. Schmidt, G. Pfleiderer and F. Bartkowiak; "Synthesis and properties of 5-membered heterocyclic disulfides: application for enzyme modification." *Ana. Biochem., **138(1)**, 217-22, (1984).*

[31] M. Patel and M. Braden; "Heterocyclic methacrylates for clinical applications.III. Water absorption characteristics." *Biomat., **12(7)**, 653-7, (1991).*

[32] M. Gaston, L. Dias, A. Freitas, A. Miranda and E. Barrerio; "Synthesis and analgesic properties of new 4-arylhydrazone 1-H pyrazole [3,4-b] pyridine derivatives." *Pharmaceut. acta Helvetiae, **71(3)**, 213-9, (1996).*

[33] R. Naik and K. Desai; "Heterocyclic azo dyes: synthesis of styryl pyrazolone azo dyes and their application on various textile fibers as acid dyes." *Oriental J. Chem., **14(1)**, 161-62, (1998).*

[34] B. Kundu, S. Bijoy, D. Sawant, P. Partani and A. Kesarwani; "New application of Pictet-pengler reaction leading to the synthesis of an unusual seven-membered heterocyclic ring system." *J. Org. Chem., **70(12)**, 4889-92, (2005).*

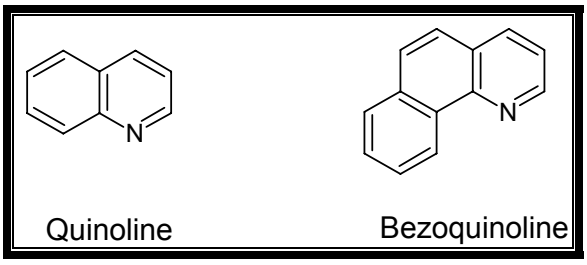
[35] W. Jones; "Diverse Chemical Applications of N- Heterocyclic Carbenes." *J. Am. Chem. Soc., **131(42)**, 15075-77, (2009).*

INTRODUCTION

Quinolines are heterocyclic aromatic organic compounds containing nitrogen. These heterocycles are promising for use in practical applications.

The synthesis of quinolines and their derivatives has been of considerable interest because a large number of natural products and drugs contain this heterocyclic unit.

These compounds are also used as building blocks of various other compounds such as benzoquinoline. Various other compounds such as chalcones[1-5], pyrazolines, acetyl pyrazolines, phenyl pyrazolines[6-8], cyanopyridines[9,12], isoxazoles [12-16], thiazolidinones[17-20], azetidinones[21-24], sulphonamides[25-27], arylamides [28-31], thiopyrimidines[32-35], amino pyarimidines[36-41], benzodiazepines[42-44] , azomethines[45-50] etc. also contain this heterocyclic ring.



Due to biological activities of above class of compounds, benzoquinoline derivatives of some selected compounds such like cyanopyridines, aminopyrimidines, 1,5- benzodiazepines, pyrazolines and sulphonamides have been synthesized in this work.

Different methods have been reported for the synthesis of quinoline[51-53], benzoquinoline[54-59] and other quinoline derivatives[60-67].

It is well known that cyanopyridines have a broad spectrum of biological activity such as anticonvulsant[68-69], fungicidal[70], analgesic[71-72], anti-inflammatory[73-74], anticancer[75-76], antihypertensive[77-78], insecticidal [79-80], antiulcer[81-82], antitubercular[83], molluscicidal[84] etc. Graciunescu et al.[85] have reported antiepileptic activities and toxicological profiles of some complex salts of pyridine derivatives. The anti-inflammatory activities of some cyanopyridines have also been studied by Moeller and Gloxhuber[86]. The antihypertensive[87], insecticidal[88] and antianexiety[89] activity of these derivatives have also been reported. Further, the antimicrobial activity of some of these derivatives has been studied by various workers[90-94].

Literature survey shows that Amino pyrimidine derivatives also exhibit various biological activities[95-101]. Buschauer[100] has reported their antihistaminic activity whereas anthelmintic activity[101] has been reported by Chalquest. The antimicrobial activities of a variety of these amino pyrimidines have been studied by various workers[102-105]. The cytokinin activitywas reported by Takahashi et al.[106] whereas some of them also act as insecticide[107]. The pesticidal and fungicidal activity of some amino pyrimidine derivatives have also been reported.[108-110]

Further, benzodiazepine derivatives are known to have biological activities such as anticonvulsant[111], CNS active agent[112], neuroleptic[113], antihypertensive[114], antiproliferative[115], anti-inflammatory [116], cardiovascular[117], antiamnesic[118], antimicrobial[119], anthelmintic[120] etc.

Hester[121] has reported sedative and antispasmodic effect of some triazole-benzodiazepines. The Psychotropic[122] and antibiotics[123] activity of some benzodiazepines have also been reported. Golik[124] has also reported 2,4-benzodiazepine as a potent CNS agent. The structure-activity relationship studies of some benzodiazepines as oxytocin antagonist have been documented[125]. The antimicrobial, antifungal and anthelmintic activities of 3H-1,5-benzodiazepine derivatives have been studied by Kumar et al[126]. Further, many workers[127-129] have been reported other biologically active benzodiazepines.

Pyrazoline derivatives have been found to possess wide range of therapeutic activities such as antidiabetic[130], insecticidal[131-133] tranquilizer [134], hypoglycemic[135], anti-inflammatory[136-137], anticonvulsant[138], diuretics [139], analgesic[140], anti HIV[141], anticancer[142], antituberculosis[143], etc. Recently, antimicrobial activities of some novel pyrazolines have been reported by Jadhav et al.[144].

The discovery of sulphonamides marked the beginning of chemotherapeutic era by making possible a direct attack on microbial infections[145]. Sulphonamide antibacterials continue to be used because they are effective, inexpensive and free of infection problems of the broad spectrum antibiotics[146].

Literature survey shows that Loh and co-workers have prepared substituted benzene sulphonyl hydrazones which caused disappearance of

tumor in 20-80% of leukemia bearing mice[147]. Fagerlund and co-workers have studied diuretic sulphonamides[148]. It's applications on Cadiovascular, inflammatory, pulmonary and diabetes related diseases have been reported by Gless[149]. Crocetti et al.[150] have found some substituted derivatives of sulphonamides as anathematic agent. Further, antihypertensive, antibiotics, antimalaric, antimicrobial, diuretics, hypoglycemics, antiinflammatory properties of this magic group of compounds have also been studied by Brana et al.[151].

Moreover, in vitro antiarthramic[152], anti HIV[153], herbicidal[154], anti viral[155], antifungal[156], hypotensive[157] and anticoagulant[158] activities for sulphonamides has been reported. Recently, antimicrobial activity of sunlphonamide complexes has been studied by Nair et al.[159].

Thus, due to wide spectrum of biological activities of various compounds having benzoquinoline moiety, in the present work, some new derivatives such as cyanopyridines, amonopyrimidines, benzodiazepines, pyrazolines and sulphonamides are designed as potential compounds.

REFERENCES

[1] N. Fathy, A. Aly, F. Abdel-Motti F. Abdel-Megeid; "Some reactions with 3-(2-chloro-7-methylquinolinyl) chalcone derivatives." *J. Chin. Chem. Soc., **35(5)**, 365-72, (1988).*

[2] R. Li, X. Chen, B. Gong, J. Dominguez, E. Davidson, G. Kurzban, R. Miller, E. Nuzum, P. Rosenthal; "In Vitro Antimalarial Activity of Chalcones and Their Derivatives." *J. Med. Chem., (1995),* ***38(26)****, 5031-7.*

[3] M. Cheng, R. Li, G. Kenyon; "A solid phase synthesis of chalcones by Claisen-Schmidt condensations." *Chin. Chem. Let.,* ***11(10)****, 851-54, (2000).*

[4] A. Bouraiou, H. Menasra, A. Debache, S. Rhouati, A. Belfaitah; "Synthesis of some functionalized quinolylaziridine derivatives." *J. Soc. Alger. Chim.,* ***16(2)****, 171-83, (2006).*

[5] E. Hamad, S. Abdel-Sattar; "Synthesis and characterization of pyrido[1,2-a]quinoline palladacycles." *Mona. Chem.,* ***139(11)****, 1285-97 (2008)*.

[6] R. Srivastava, B. Neelima; "Reactions of 2-chloro-3-formylquinolines." *Ind. J. Chem.,* ***26B(5)****, 418-22, (1987).*

[7] F. Bharmal, D. Kaneriya, H. Parekh; "Synthesis of some pyrazoline derivatives as biologically active agents." *Ind. J. Hetero. Chem.,* ***10(3)****, 189-92, (2001).*

[8] F. Bharmal, D. Kaneriya; "Synthesis and biological activity of some pyrazolines." *Ind. J. Hetero. Chem.,* ***12(1)****, 21-24, (2002).*

[9] F. Villani, J. Hannon, E. Wefer, T. Mann, J. Morton; "Benzopyranopyridine derivatives. 2. Reaction of azaxanthones with hydroxylamine." *J. Org. Chem.,* ***40(12)****, 1734-7, (1975).*

[10] R. Khunt, N. Datta, F. Bharmal, G. Mankad, A. Parikh; "Synthesis and biological evaluation of cyanopyridine and isoxazole derivatives." *Ind. J. Hetero. Chem.,* ***10(2)****, 97-100 (2000).*

[11] N. Datta, R. Khunt, A. Parikh; "Synthesis of pyrimidinethiones and cyanopyridines as biologically active agents." *Orient. J. Chem.,* ***18(1)****, 131-134, (2002).*

[12] R. Khunt, N. Datta, F. Bharmal, G. Mankad, A. Parikh; "Synthesis and biological evaluation of cyanopyridine and isoxazole derivatives." *Ind. J. Hetero. Chem.,* ***10(2)****, 97-100, (2000).*

[13] M. Zhenkun, L. Tam, R. Clark, S. Zhang, S. Djuric; "Preparation of antibacterial 6-O-substituted erythromycin derivatives having improved gastrointestinal tolerance." PCT Int. Appl., 73, (2002).

[14] A. Dobaria, J. Patel, H. Parekh; "Synthesis of pyrazoline and isoxazole derivatives bearing a chloroquinoline nucleus as potential antimicrobial agents." *Ind. J. Chem.,* ***42B(8)****, 2019-22 (2003).*

[15] T. Nowak, A. Thomas; "Preparation of 4-(pyrazol-3-ylamino)pyrimidines for use in the treatment of cancer." PCT Int., 272, (2005).

[16] A. Thomas, T. Nowak; "Preparation of 4-(pyrid-2-yl)amino substituted pyrimidines as therapeutic protein kinase inhibitors." PCT Int., 118, (2006).

[17] B. Kansagra, H. Bhatt, A. Parikh; "Synthesis and antimicrobial activity of substituted 4-thiazolidinones bearing 2-chloroquinoline nucleus." *Ind. J. Hetero. Chem.,* ***10(1)****, 5-8 (2000).*

[18] G. Selvi, S. Rajendran; "Synthesis of some new 2-[3-(2-chloroquinolinyl)]-3-aryl-4-thiazolidi nones as potent antibacterial agents." *Asian J. Chem., **16(2)**,1017-22 (2004)*.

[19] G. Selvi, S. Rajendran, "Synthesis of 2-[3'(2'-chloroquinolinyl)-3-carbethoxy methyl]-4-thiazolidinones." Ind. J. Hetero. Chem., ***17(2)***, 201-02, (2007).

[20] P. Rana, B. Mistry, K. Desai; "Green chemistry: conventional and microwave induced synthesis of various thiazolidinone derivatives from 3-{[(1E)-(2'-chloro-7'-methoxy quinoline-3'-yl)methylene]amino}-4-(substituted phenyldiazenyl)phenol and their anti microbial screening." *ARKIVOC, **(15)**, 262-79, (2008).*

[21] B. Kansagra, H. Bhatt, A. Parikh; "Synthesis and biological screening of some azomethines and 2-azetidinones." *J. Inst. Chem., **72(2)**, 68-69, (2000)*

[22] F. Bharmal, D. Kaneriya, H. Parekh; "Synthesis of 2-Azetidinones from 2-chloro-8-methyl-3-quinolinecarbaldehyde as potential antimicrobial agents." *Orient. J. Chem., **18(1)**, 89-92, (2002).*

[23] S. Junne, S. Wajde, M. Baig, Y. Vibhute, "Novel heterocyclic schiff bases, 4-thiazolidinones and 2-azetidinones possessing antibacterial and antifungal activity." *Intt. J. Chem. Sci., **5(5)**, 2093-01, (2007).*

[24] J. Patel, B. Mistry, K. Desai, "Conventional and microwave induced synthesis of various azetidinone and thiazolidinone derivatives from 3-[(1E)-1-aza-2-(2-chloro-7-methoxy-3-quinolyl)-vinyl]-4-(aryldiazenyl)phenol and their antimicrobial screening." *Ind. J. Chem., **47B(11)**, 1695-1700, (2008).*

[25] N. Fathy, A. Aly, F. Abd-El-Motti, F. Abdel-Megeid; "Some reactions of 2-chloro quinoline-3-carbaldehydes." *J. Chem., **29(5)**, 609-15, (1987).*

[26] R. Khunt, N. Datta, Neela, F. Bharmal, A. Parikh, "Sulfonamides: synthesis and antimicrobial activity of N-arylsulfonamido-2-chloro-7-methoxyquinolin-3-yl-azomethine." *J. Insti.. Chem., **72(3)**, 99-101, (2000).*

[27] N. Suryakiran, P. Prabhakar, Y. Venkateswarlu; "Synthesis of 3-amino-substituted N-alkylindazoles via palladium(II)-catalyzed intramolecular N-arylation of tosylhydrazines." *Chem. Lett., **36(11)**, 1370-71, (2007).*

[28] N. Fathy, A. Aly, F. Abd-El-Motti, F. Abdel-Megeid; "Some reactions of 2-chloro quinoline-3-carbaldehydes." *J. Chem., **29(5)**, 609-15, (1987).*

[29] E. Taylor, D. Sobieray; "Bicyclobenzodiazepinones from 3-oxo-1,2-diazetidinium hydroxide, inner salts." *Tetrahedron, **47(46)**, 9599-620, (1991).*

[30] M. Amir, S. Khan, S. Alam, S. Shahni; "Synthesis and anti-inflammatory activity of some new hydrazones of aryl alkanoic acid." *Ind. Drugs, **38(10)**, 518-22, (2001).*

[31] T. Volovnenko, A. Tarasov, Y. Volovenko; "Reactions of 1-aryl-3-chloroisoquinoline-4-carbaldehydes with C- and N-nucleophiles." *Ukrainskii Khimicheskii Zhurnal, **74(11-12)**, 44-51, (2008).*

[32] M. Kidwai, S. Saxena, R. Mohan, R. Venkataramanan; "A novel one pot synthesis of nitrogen containing heterocycles: an alternate methodology to the Biginelli and Hantzsch reactions." *J. Chem. Soc., Perkin Trans.,* ***1,(16)****, 1845-46, (2002).*

[33] M. Kidwai, S. Saxena, M. Khan, R. Khalilur, S. Thukral; "Synthesis of 4-aryl-7,7-dimethyl-1,2,3,4,5,6,7,8-octahydroquinazoline-2-one/thione-5-one derivatives and evaluation as antibacterials." *Eur. J. Med. Chem.,* ***40(8)****, 816-19, (2005).*

[34] R. Gupta, M. Gupta, S. Paul, R. Gupta; "Silica-supported ZnCl2 - A highly active and reusable heterogeneous catalyst for the one-pot synthesis of dihydropyrimidinones-thiones." *Can. J. Chem.,* ***85(3)****, 197-201, (2007).*

[35] S. Ramalingam, P. Kumar; "Yttria-zirconia-based Lewis acid catalysis of the Biginelli reaction. An efficient one-pot synthesis of 3,4-dihydropyrimidin-2-(1H)-ones." *Syn. Commun.,* ***39(7)****, 1299-09, (2009).*

[36] G. Bennett, R. Mason, L. Alden, J. Roach; "Synthesis and antiinflammatory activity of trisubstituted pyrimidines and triazines." *J. Med. Chem.,* ***21(7)****, 623-8, (1978).*

[37] J. Gillessen; "Antimycotic substances. XX. Fluorinated 2-(4-toluidino)pyrimidines." A. Kreutzberger, *J. Hetero. Chem.,* ***22(1)****, 101-3, (1985).*

[38] R. Paul, W. Hallett, J. Hanifin, M. Reich, B. Johnson, R. Lenhard, J. Dusza, S. Kerwar, Y. Lin; "Preparation of substituted N-phenyl-4-aryl-2-pyrimidinamines as mediator release inhibitors." *J. Med. Chem.,* ***36(19)****, 2716-25, (1993).*

[39] B. Hodous, M. Geuns, D. Stephanie, P. Hughes, B. Albrecht, S. Bellon, C. James, C. Sean, J Victor, S. Chaffee; "Evolution of a Highly Selective and Potent 2-(Pyridin-2-yl)-1,3,5-triazine Tie-2 Kinase Inhibitor." *J. Med. Chem.,* ***50(4)****, 611-626, (2007).*

[40] Tamayo, Nuria; Liao, Hongyu; Stec, Markian M.; "Design and Synthesis of Peripherally Restricted Transient Receptor Potential Vanilloid 1 (TRPV1) Antagonists." *J. Med. Chem.,* ***51(9)****, 2744-57, (2008).*

[41] S. Ioannidis, M. Lamb, "Preparation of N-(pyrazol-3-yl)-N'-(1-pyridin-2-ylethyl) pyrimidine-2,4-diamine derivatives as JAK inhibitors for the treatment of cancer." PCT Int. Appl., 73, (2009).

[42] S. Kulkarni, K. Thakar, "Synthesis of some 1,5-benzodiazepines, Part II." J. Ind. Chem. Soc., ***53(3)***, 279-82, (1976).

[43] V. Bozhanov, S. Ivonin; "Synthesis of 4-pyridyl-2,3-dihydro-1H-1,5-benzodiazepin-2-ones." Chem. Hetero. Comp., ***38(9)***, 1098-03, (2002).

[44] B. Willy, T. Dallos, F. Rominger, J. Schonhaber, T. Mueller; "Three-component synthesis of cryofluorescent 2,4-disubstituted 3H-1,5-2 benzodiazepines - conformational control of emission properties." *Eur. J. Org. Chem.,* ***(28)****, 4796-4805, (2008).*

[45] R. Gatti, V. Cavrini, M. Cesaroni, P. Roveri, P. Brigidi; "Synthesis and antibacterial activity of azomethine and aminomethyl analogs of 2,7-dimethoxyquinoline-3-carboxaldehydes." Bollettino Chim. Farmaceutico, ***124(2)***, 69-74, (1985).

[46] Z. Pagani, I. Torrini, P. Paglialunga; "Synthesis of quino[2,3-b][1,5]benzoxazepines: a novel tetracyclic ring system." *Heterocycles, **26(9)**, 2443-7, (1987).*

[47] E. Mohamed, M. Ismail, Y. Gabr, H. Farrag; "Synthesis and biological activity of some 3-heterocyclyl-4-hydroxy-6-methyl-2 (1H)-quinolones." Ind. J. Chem., ***34B(1)***, 21-6, (1995).

[48] B. Kansagra, H. Bhatt, A. Parikh; "Synthesis and antimicrobial activity of substituted 4-thiazolidinones bearing 2-chloroquinoline nucleus." Ind. J. Hetero. Chem., ***10(1)***, 5-8, (2000).

[49] A. Srivastava, R. Singh; "Vilsmeier-Haack reagent: A facile synthesis of 2-chloro-3-formylquinolines from N-arylacetamides and transformation into different functionalities." Ind. J. Chem., ***44B(9)***, 1868-75, (2005).

[50] J. Patel, B. Mistry, K. Desai, "Conventional and microwave induced synthesis of various azetidinone and thiazolidinone derivatives from 3-[(1E)-1-aza-2-(2-chloro-7-methoxy-3-quinolyl)-vinyl]-4-(aryldiazenyl)phenol and their antimicrobial screening." *Ind. J. Chem., **47B(11)**, 1695-1700, (2008).*

[51] Z. H. Skraup; "Eine Synthese des Chinolins". *Berichte **13**, 2086, (1880).*

[52] L. Knorr "Synthetische Versuche mit dem Acetessigester." *Justus Liebig's Annalen der Chemie, **236(1-2)**, 69-115 (1886).*

[53] O.Doebner; *Ann., **242**, 265, (1887).*

[54] N. N.Vorozhtsov, S. I. Kutkevichus; "Products of reaction of epichlorohydrin with aromatic amines. III. Action of hydrochloric acid and thionyl chloride on 3-hydroxy-1,2,3,4- tetrahydro-7,8-benzoquinoline and 3-hydroxy-1,2,3,4-tetrahydro-5,6-benzo quinoline. " *Z. Obshchei Khimii, **28**, 2682-87, (1958).*

[55] P. Singh, N. Singh; "Chemistry of benzoquinolines. Part VI." *J. Ind. Chem. Soc., **52(11),** 1108-9, (1975)*

[56] Y. Hamada, I. Takeuchi; "Syntheses of nitrogen-containing heterocyclic compounds. 26. Reaction of benzo[f or h]quinolines and their N-oxides with methylsulfinyl carbanion." *J. Org. Chem., **42(26)**, 4209-13, (1977).*

[57] Z. Zhang, J. Chen; "Synthesis of 7,8-benzoquinoline." *Huaxue Shiji, **12(5)**, 313(1990).*

[58] C. Cho, D. Kim, T. Kim, S. Shim; "Ruthenium-catalyzed synthesis of quinolines from anilines and tris(3-hydroxypropyl)amine via amine exchange reaction." *Bull. Korean Chem. Soc., **24(7)**, 1026-28, (2003).*

[59] H. Aramoto, Y. Obora, Y. Ishii; "N-Heterocyclization of Naphthylamines with 1,2- and 1,3- Diols Catalyzed by an Iridium Chloride/BINAP System." *J. Org. Chem., **74(2),** 628-33,* (2009).

[60] A. Mustafa, A. Mansour, A. Shalaby,; "Photochemical reactions in sunlight. Experiments with benzo[h]quinoline-5,6-quinone, monoimine and monoxime derivatives in sunlight and in dark." *J. Am. Chem. Soc., **81**, 3409-13, (1959).*

[61] *G. Hall, J. Walker;* "Ring-closure to phenanthridines and acridines of some 2-arylaminomethylene derivatives of cyclohexanone and 1-tetralone." *J. Chem. Soc., **(17)**, 2237-44, (1968).*

[62] P. Singh, N. Singh; "Reactions and synthesis of 2,4-dimethyl-7,8-benzoquinoline." *Ind. J. Chem., **12(9)**, 1016-17, (1974).*

[63] R. Lehr, S. Kumar; "Synthesis of dihydrodiol and other derivatives of benz[c]acridine." *J. Org. Chem., **46(18)**, 3675-81, (1981).*

[64] R. Goehring; "An exceptionally brief synthesis of eupolauramine." *Tetrahedron Let., **33(41)**, 6045-8, (1992).*

[65] Z. Wrobel; "Silane-mediated direct condensation of nitroarenes with cinnamyl-type sulfones. The way to 2-aryl-4-X-quinolines and their hetero analogs." *Tetrahedron, **54(11)**, 2607-18, (1998).*

[66] T. Harayama, S. Takashi, N. Tomonori, H. Abe, Y. Takeuchi; "Concise synthesis of fagaridine and decarine, phenolic benzo[c]phenanthridine alkaloids, using the palladium-assisted biaryl coupling reaction." *Heterocycles, **59(1)**, 293-301, (2003).*

[67] K. Kim, H. Lee, K. Seung; "Synthesis of 3,4-disubstituted 2(1H)-quinolinones via intramolecular Friedel-Crafts reaction of N-arylamides of Baylis-Hillman adducts." *Tetrahedron Let., **50(11)**, 1249-51, (2009).*

[68] A. G. Chapman, K. Nanan, M. Williams, B. S. Meldrum; "Anticonvulsant activity of two metabotropic glutamate Group I antagonists selective for the mGlu5 receptor: 2-methyl-6-(phenylethynyl)- pyridine (MPEP), and (E)-6-methyl-2-styryl- pyridine" (SIB 1893), *Neuropharmaco*., ***39***, *1567-74 (2000).*

[69] E. G. Paronikyan, S. N. Sirakanyan, A. S. Noravyan, R. G. Paronikyan, N. E. Akopyan; "5-Substituted 1-amino-8,9-dihydro-8,8-dimethyl-3H,6H-pyrazolo[3,4-b] pyrano[4',3'-d] pyridine or their hydrochlorides showing anticonvulsant activity.", *U.S.S.R. (1995).*

[70] T. Umeda, S. Onoe, M. Kusunoki, S. Kutsuma, Y. Noshiro, C. Ono, Y. Watanabe; "Preparation of cyanopyridine derivatives as intermediates for agrochemical fungicides." *Jpn. Kokai Tokkyo Koho., 18, (1997).*

[71] S. M. Sondhi, S. Jain, M. Dinodia, A. Kumar; "Synthesis of some thiophene, imidazole and pyridine derivatives exhibiting good anti-inflammatory and analgesic activities." *Med. Chem*., ***4**, 146-54 (2008).*

[72] I. Muszalska, E. Wojtyniak; "Stability of new analgesic active compound,pyrrolo-[3,4-c] pyridine derivative, in aqueous solutions." *Acta Polo. Pharm*., ***64**, 319-25 (2007).*

[73] B. M. Klebanov, T. K. Ryabukha, V. A. Portnyagina, V. F. Danilenko, G. A. Get'man; **"**Antiinflammatory activity of some new pyridine carboxylic acid derivatives." *Fizi. Akti. Vesh*., ***9***, *17-19 (1977).*

[74] T. Birkinshaw, S. Connolly, T. Luker, A. Mete, I. Millichip; "Preparation of arylheteroalkylamine derivatives as nitric oxide synthase inhibitors useful as anti - inflammatories and analgesics." 123, *PCT Int. Appl*., *(2002).*

[75] W. Hu, N. Sun, Z. Yang; "Synthesis and anticancer activity of thiosemi- carbazones." *Gao. Xu. Hu. Xu*., ***22***, *2014-17 (2001).*

[76] M. M. Ghorab, S. G. Abdel-Hamide, M. M. Abou Zeid; "Synthesis of some new thiadiazole, selena, triazine, thiazole and cyanopyridine derivatives with assay for their antitumor activity." *Phosphorus, Sulfur, Silicon Rel. Ele*., ***112***, *7-17 (1996).*

[77] Y. Ozaki, Y. Yamamura, T. Noguchi; "Stable freeze-dried preparations containing antihypertensive 1,4-dihydropyridine derivative for injection." *Jpn. Kokai Tokkyo Koho*., *3, (1993).*

[78] I. Matsumoto, K. Nakagawa, M. Matsuzaki, K. Horiuchi; "Antihypertensive 2,6-bis [[(thiocarbamoyl)thio]methyl] pyridine." *Ger. Offen*., ***19***, *(1972).*

[79] M. H. Khan, R. Haque, A. Safi, Nizamuddin; "Synthesis and insecticidal activity of 3-substituted 5-amino-7-aryl-6-cyano-2,3,4,7-tetrahydrothiazolo[4,5-b] pyridine-2-thiones and 3-substituted 7-aryl-6-cyano-2,3,4,5,6,7-hexahydro-2-thioxothiazolo[4,5-b]pyridin-5-ones." *Ind. J. Chem*., ***37***, *1069-74 (1998).*

[80] F. Sun, D. Shi; "Insecticidal activity of some new amidophosphoric acid esters containing substituted pyridine moieties." *Phosphorus, Sulfur, Silicon Rel. Ele*., ***183***, *2615-20 (2008).*

[81] F. Hirayama, Y. Yokoyama, K. Ikeda, M. Sano, T. Kawakita; "Combined use of pyridine derivatives as Helicobacter pylori inhibitors and antiulcer agents." *Jpn. Kokai Tokkyo Koho.,* 9, (1998),

[82] S. Y. Tzou, S. Chen, S. Chen; "Preparation of pyridine derivatives as intermediates for antiulcer omeprazole.", 4, *Taiwan (2001).*

[83] V. V. Kachhadia, M. R. Patel, H. S. Joshi; "Synthesis of isoxazoles and cyanopyridines bearing benzo(b)thiophene nucleus as potential antitubercular and antimicrobial agents." *J. Sci. Islamic Rep. Iran*., ***15***, *47-51(2004).*

[84] N. Latif, F. M. Asaad, N. S. Girgis; "Malononitriles and cyano esters: Part VII - Diaryl- and dithienylpropenones and -cyanopyridines and their molluscicidal activity.", *Ind. J. Chem*., ***20***, *463-66 (1981).*

[85] D. G. Graciunescu, M. T. Gutierrez Rios, E. Parrondo, C. Molina, A. Doadrio, C. Guirvu; "Studies on the antiepileptic activities and toxicological profiles of some complex salts of $[Cu(II)Br_4](LH)_2$ where L=a pyridine derivative.", *Anal. Real Acad. Farm*., ***55***, *329-38 (1989).*

[86] H. Moeller, C. Gloxhuber; "Antiinflammatory 2-cyano-1,2-dihydro-1-(benzoxazol-2-yl)pyridines.", *Ger. Offen*., *18, (1974).*

[87] J. J. Baldwin, E. L. Engelhardt, R. Hirschmann, G. S. Ponticello, J. G. Atkinson, B. K. Wasson, C. S. Sweet, A. Scriabine; "Heterocyclic analogs of the antihypertensive β - adrenergic blocking agent (S)-2-[3-(tert-butylamino)-2-hydroxypropoxy]-3-cyano pyridine.", *J. Med. Chem*., ***23***, *65-70 (1980).*

[88] N. Sakamoto, T. Ishiwatari, N. Matsuo; "Synthesis and insecticidal activit of [1(2H),2'-bipyridine]-2-one derivatives." *Nipp. Noy. Gakk*., ***25***, *373-78 (2000).*

[89] Amr, S. F. Mohamed, N. A. Abdel-Hafez, M. M. Abdalla; "Antianexiety activity of pyridine derivatives synthesized from 2-chloro-6-hydrazino-isonicotinic acid hydrazide." *Mona. Chemie*., ***139***, *1491-98 (2008).*

[90] N. Z. Tugusheva, L. V. Ershov, V. G. Granik, G. Y. Shvarts, R. D. Syubaev, M. D. Mashkovskii; "Synthesis and biological activity of mono- and tricyclic derivatives of 2-amino-3-cyanopyridine." *Khim. Farm. Zhur*., ***20***, *830-35 (1986).*

[91] S. Ganguly, M. Vadodaria, A. R. Parikh; "Synthesis and biological evaluation of cyanopyridine derivatives bearing a phenylsulfonamidophenyl moiety." *J. Inst. Chem*. ***68***, *46-48 (1996).*

[92] V. B. Patel, S. D. Sorathiya, A. R. Parikh; "Synthesis of some novel cyanopyridines and isoxazoles bearing sulfonamide moiety and their antimicrobial activity." *Ind. J. Chem*., ***36***, *822-25 (1997).*

[93] B. P. Kansagra, H. H. Bhatt, A. R. Parikh; "Synthesis and antimicrobial activity of some isoxazoles and cyanopyridines." *Ind. J. Hetero. Chem*., ***12***, *61-64 (2002).*

[94] J. M. Desai, V. H. Shah; "Synthesis and biological activity of cyanopyridine, isoxazole and pyrazoline derivatives having thymol moiety." *Ind. J. Chem*., ***42***, *382-85 (2003).*

[95] R. Huang, G. Xu, M. Gaul, S. Emanuel, K. Lamontagne, L. Greenberger; "Synthesis and biological study of 4-aminopyrimidine-5-carbo-xaldehyde oximes as antiprolifera tive VEGFR-2 inhibitors." *Biorg. Med. Chem. Lett*., ***16***, *6063-66 (2006).*

[96] D. Wustrow, T. Belliotti, S. Glase, S. R. Kesten, D. Johnson, N. Colbry; "Aminopyrimidines with high affinity for both serotonin and dopamine receptors." *J. Med. Chem*., ***41***, *760-71 (1998).*

[97] M. Okada, T. Yoden, E. Kawaminami, Y. Shimada, M. Kudoh, Y. Isomura; "Studies on aromatase inhibitors. IV. Synthesis and biological evaluation of N,N-disubstituted-5-aminopyrimidine derivatives. " *Chem. Pharm. Bull*., ***45***, *1293-99 (1997)*.

[98] S. A. Ouf, S. M. Sherif; "Synthesis and fungitoxicity of some pyrimidine derivatives. " *Folia Microbiol*., ***38***, *181-7 (1993)*.

[99] Z. H. Chohan, S. Kausar; "Biologically active complexes of nickel(II), copper(II) and zinc(II) with Schiff-base ligand derived from the reaction of 2-aminopyridine and pyrrol-2-carboxaldehyde-their synthesis and characterization. " *Chem. Pharm. Bull.,* ***40***, 2555-56 (1992).

[100] A. Buschauer; "4-Aminopyrimidines with H2-antihistaminic activity. " *Pharma. Zeit*., ***130***, *2067-70 (1985).*

[101] R. R. Chalquest; "4-Phenoxy-6-aminopyrimidine derivative anthelmintics and nematocides. " *PCT Int. Appl., 91(2001).*

[102] M. Ghannoum, K. Abu N. El-Rayyes;"Antimicrobial activity of some 2-aminopyrimidines. " *Microbios*., ***60***, *23-33 (1989).*

[103] V. B. Kadu, A. G. Doshi; "Synthesis and antimicrobial activity of 2-amino-4-(2-hydroxy-3,4-benzophenyl)-6-(substituted phenyl)pyrimidines and 2(1H)-pyrimidino nes. " *Res. J. Chem. Environ*., ***2***, *69-71 (1998).*

[104] B. Desai, S. Modi, H. Naik; "Antimicrobial studies of some new chalcones and 2-aminopyrimidines." *J. Ind. Coun. Chem*., ***10***, 11-14 (1994).

[105] A. Solankee, K. Kapadia, S. Lad, J. Patel, I. Thakor; "Synthesis and antimicrobial activity of s-triazine based chalcones, pyrazolines and aminopyrimidines. " *Asian J. Chem*., ***16***, 727-32 (2004).

[106] S. Takahashi, T. Yatsunami, K. Shudo, T. Okamoto, K. Yamada, Y. Isogai; "Cytokinin activity of pyrimidine derivatives. " *Chem. Pharma. Bull*., ***26***, 2286-87 (1978).

[107] H. Yoshioka, T. Obata, K. Fujii, H. Yoshiya, K. Tsutsumiuchi; "Preparation of aminopyrimidine derivative as insecticide and acaricide. " *Jpn. Kokai Tokkyo Koho*., *6 (1990).*

[108] T. Obata, K. Fujii, I. Narita, S. Shikita; "Preparation of aminopyrimidine derivatives as pesticides and fungicides. ", *Eur. Pat. Appl*., *41, (1991).*

[109] J. Drumm; "Preparation of fungicidal and miticidal and arthropodicidal aminopyri midine agrochemicals." *PCT Int. Appl*., 88*, (1995).*

[110] D. V. Singh, A. R. Mishra, R. M. Mishra, A. K. Pandey, C. R. Singh, A. K. Dwivedi, "Synthesis and fungicidal activity of benzofuran incorporated substituted pyrimidines." *Ind. J. Hetero. Chem*., ***14,*** *319-22 (2005).*

[111] A. M. Fatmi; "Synthesis of benzodiazepines and dihydroquinazolines as potential anticonvulsant agents." *Avail. Univ. Microfilms Int., Order No.8201535*, *108 pp (1981).*

[112] V. K. Srivastava, R. K. Satsangi, K. Kishore; "2-(2'-Hydroxyphenyl)-4-aryl-1,5-benzodiazepines as CNS active agents." *Arzn. Fors*., ***32***, *1512-14 (1982)*.

[113] J. K. Chakrabarti, J. Fairhurst, N. Gutteridge, L. Horsman, I. Pullar, C. W. Smith, D. Steggles, D. E. Tupper, F. C. Wright; "Heteroarenobenzodiazepines: 10-Piperazinyl-4H-thieno[3,2-b][1,5]- and -[3,4-b][1,5]benzodiazepines as potential neuroleptics." *J. Med. Chem*., ***23***, 884-9 (1980).

[114] L. L. Setescak, F. W. Dekow, J. Kitzen, L. Martin; "4-Aryl-4,5-dihydro-3H-1,3-benzodiazepines: 2-Phenyl and 2-amino analogs as potential antihypertensive agents." *J. Med. Chem*., ***27***, *401-04 (1984).*

[115] W. Nawrocka, B. Sztuba, A. Opolski, J. Wietrzyk, M. Kowalska, T. Glowiak; "Synthesis and antiproliferative activity in vitro of novel 1,5-benzodiazepines." *Archiv. Pharm*., ***334***, *3-10 (2001).*

[116] G. Grossi, M. Braccio, G. Roma, V. Ballabeni, M. Tognolini, F. Calcina, E. Barocelli; "1,5-benzodiazepines: Part XIII. Substituted 4H-[1,2,4]triazolo[4,3-a][1,5]benzo diazepin-5-amines and 4H-imidazo[1,2-a][1,5]benzodiazepin-5-amines as analgesic, anti-inflammatory and/or antipyretic agents with low acute toxicity." *Euro. J. Med. Chem*., ***37***, *933-44 (2002).*

[117] S. Shukla, U. Misra, M. Bhalla, D. Mukerjee, A. K. Saxena, J. N. Sinha, K. Shanker; "Biologically active substituted benzodiazepines and their effect on cardiovascular and central nervous system." *Boll. Chim. Farm*., ***140***, *53-58 (2001).*

[118] M. Anzini, L. Canullo, C. Braile, A. Cappelli, A. Gallelli, S. Vomero, M. Menziani;

"Synthesis, biological evaluation, and receptor docking simulations of 2-[(Acylamino)ethyl]-1,4-benzodiazepines as opioid receptor agonists endowed with antinociceptive and antiamnesic activity." *J. Med. Chem.*, ***46***, *3853-64 (2003).*

[119] R. Kumar, Y. Joshi; "Synthesis, spectral studies and biological activity of novel 3H-1,5-benzodiazepine derivatives." *Ind. J. Chem.*, ***46***, *2021-25 (2007).*

[120] R. Kumar, Y. Joshi; "Synthesis and antimicrobial, antifungal and anthelmintic activities of 3H-1,5- benzodiazepine derivatives." J. Serb. Chem. Soc., ***73(10)***, *937-43 (2008).*

[121] B. Hester; "Sedative and antispasmodic 6-phenyl-4H-s-triazolo[4,3-a][1,4] benzo diazepines." *Ger. Offen.*, *36,* (1970).

[122] A. Bauer, P. Danneberg, K. Weber, K. Minck; „Benzodiazepines with psychotropic activity. Synthesis and biological action of 4-amino-1,5- benzodiazepines." *J. Med. Chem.*, ***16***, 1011-14 (1973).

[123] A. Kamal, M. Rao, N. Laxman, G. Ramesh, G. S. Reddy; "Recent developments in the design, synthesis and structure-activity relationship studies of pyrrolo[2,1-c][1,4]benzodiazepines as DNA-interactive antitumor antibiotics." *Curr. Med. Chem: Anti-Cancer Agents.*, ***2***, *215-54 (2002).*

[124] U. Golik; "Synthesis of some 2,4- benzodiazepin -1-ones, potent CNS [central nervous system] agents." *J. Hetero. Chem.*, ***12***, *903-08 (1975).*

[125] P. G. Wyatt, M. J. Allen, J. Chilcott, G. Hickin, N. D. Miller, P. M. Woollard; "Structure-activity relationship investigations of a potent and selective benzodiazepine oxytocin antagonist." *Bioorg. Med. Chem. Lett.*, ***11***, *1301-05 (2001).*

[126] R. Kumar, Y. C. Joshi; "Synthesis and antimicrobial, antifungal and anthelmintic activities of 3H-1,5- benzodiazepine derivatives." *J. Serb. Chem. Soc.*, ***73***, *937-43 (2008).*

[127] A. Visnjevac, L. Tusek-Bozic, M. Majeric-Elenkov, Z. Hamersak, H. Kooijman, E. De Clercq, B. Kojic-Prodic; "Synthesis, structural characterisation and biological activity of Zn(II) and Pd(II) complexes of 3-substituted 5-(2'-pyridyl)-1,4-benzodiazepin-2-one derivatives." *Polyhedron.*, ***21***, 2567-77 (2002).

[128] A. Kamal, V. Devaiah, K. Reddy, M. Kumar; "Synthesis and biological activity of fluoroquinolone-pyrrolo[2,1-c][1,4]benzodiazepine conjugates." *Bioorg. Med. Chem.*, ***13***, *2021-29 (2005).*

[129] K. Bronisz, M. Ostafin, O. Poleshchuk, J. Mielcarek, B. Nogaj; "Studies of the electronic structure and biological activity of chosen 1,4-benzodiazepines by 35Cl NQR spectroscopy and DFT calculations." *Chem. Phy.*, ***330***, *301-06 (2006).*

[130] J. Ahn, H. Kim, S. Jung, S. Kang, K. Kim; "Synthesis and DP-IV inhibition of cyano-pyrazoline derivatives as potent anti -diabetic agents." *Bioorg. Med. Chem. Lett., **14(17)**, 4461-65, (2004).*

[131] K. Rowberg, M. Even, A. Hopfinger "QSAR and Molecular Shape Analyses of Three Series of 1-(Phenylcarbamoyl)-2- pyrazoline Insecticides." *J. Agri. Food Chem., **42(2)**, 374-80, (1994).*

[132] K. Silver, D. Soderlund; "Action of pyrazoline -type insecticides at neuronal target sites." *Pesticide Biochem. Physiology,* ***81(2)****, 136-43, (2005).*

[133] R. Chinna, R. Bardia, K. Raghubabu, S. Shrivastava; "Synthesis and insecticidal activity study of new 1-carboxamido-3-(4-naphthylsulfonylamidophenyl)-5-aryl-substituted 2- pyrazoline." *J. Insti. Chem.* ***81(2)****, 47-49, (2009).*

[134] E. Fisas, A. Maria; "Preparation of substituted pyrazoline for preventing weight gain." *Eur. Pat. Appl.,280, (2008).*

[135] M. Makki, H. Faidallah,; "Pyrazole derivatives. Part I. Synthesis and spectra of trisubstituted pyrazoline and pyrazole derivatives with possible hypoglycemic activity." *Int.. J. Chem.,* ***4(4)****, 117-28, (1993).*

[136] R. Udupi, S. Rao, A. Bhat; "Synthesis of some new pyrazoline derivatives as antimicrobial, antiinflammatory and analgesic agents." *Ind. J. Hetero. Chem.,* ***7(3)****, 217-20, (1998).*

[137] P. Kumar, P. Singh, J. Singh, A. Kumar; "Synthesis and biological activities of some indolyl substituted pyrazolines." Asian J. Chem., ***20(8)***, 6056-66, (2008).

[138] Z. Ozdemir, H. Kandilci, B. Gumusel, U. Calis, A. Bilgin; "Synthesis and studies on antidepressant and anticonvulsant activities of some 3-(2-thienyl) pyrazoline derivatives." *Arch. Pharma.,* ***341(11)****, 701-07, (2008).*

[139] Z. Brzozowski, E. Pomarnacka; "Derivatives of 4-chloro-5-sulfamoylbenzoic acid. VI. Synthesis of certain 1-(sulfamoylbenzoyl)-2- pyrazoline derivatives with expected diuretic activity." *Acta Polo. Pharma.,* ***37(4)****, 373-80, (1980).*

[140] F. Becic, D. Zavrsnik, I. Zulic, E. Becic; "Preliminary definition of analgesic effect of newly synthesized derivatives of pyrazoline and quinolinecarboxylic acids." *Periodicum Biolog.,* ***103(4)****, 321-25, (2001).*

[141] V. Jolly, M. Pathak, "Design, synthesis and biological screening of new pyrazoline derivatives." *J. Ind. Chem. Soc.,* ***68(5)****, 304-5, (1991).*

[142] D. Havrylyuk, B. Zimenkovsky, O. Vasylenko; "Synthesis of novel thiazolone-based compounds containing pyrazoline moiety and evaluation of their anticancer activity." *Eur. J. med. Chem.,* ***44(4)****, 1396-04, (2009).*

[143] B. Chetan, M. Sreenivas, A. Bhat; "Synthesis and evaluation of certain pyrazolines and related compounds for antitubercular, antibacterial and antifungal activities. " *Ind. J. Hetero. Chem.,* ***13(3)****, 225-28, (2004).*

[144] S. Jadhav, R. Shastri, K. Gaikwad, S. Gaikwad; "Synthesis and antimicrobial studies of some novel pyrazoline and isoxazoline derivatives." *E-J. Chem.,* ***6(1)****, S183-88, (2009).*

[145] R. Shepherd; "Sulphanilamides and other amino benzoic acid antagonists in medicinal chemistry.", Editor: A. Burger, (Wiley interscience), ***1***, *255, (1949).*

[146] M. Krupp and M. Chalton; "Current medicinal diagnosis and treatment", (1980).

[147] W. Loh, L. Cosby and A. Sartorelli; "Synthesis and antineoplastic activity of phenyl-substituted phenylsulfonylhydrazones of 1-pyridinecarboxaldehyde 1-oxide." *J. Med.*

*Chem., **23(6)**, 631-4, (1980).*

[148] C. Fagerlund, P. Hartvig, B. Lindstrom; "Extractive alkylation of sulphonamide diuretics and their determination by electron-capture gas chromatography." *J. Chromato., **168(1)**, 107-16, (1979).*

[149] R. Gless; "Preparation of benzenesulfonamides as soluble epoxide hydrolase inhibitors for treating cardiovascular, inflammatory, pulmonary, and diabetes-related diseases." *PCT Int. Appl., **73**, (2008).*

[150] L. Crocetti, A. Maresca, C. Temperini, R. Hall; "A thiabendazole sulfonamide shows potent inhibitory activity against mammalian and nematode carbonic anhydrases." *Bioorg. Med. Chem. Let., **19(5)**, 1371-75, (2009).*

[151] M. Brana, M. Cacho, C. Guisado; "Sulfonamides : the magic group." *Anal. Real Acad. Nacional Farma., **72(2)**, 317-41, (2006).*

[152] J. Benz, M. Kohlhardt; "Characterization of the sensitivity of cardiac outwardly-rectifying K+ channels to class III antiarrhythmics : the influence of inhibitory sulfonamide derivatives." *Nau. Schm. Arch. Pharmaco., **352(3)**, 313-21, (1995).*

[153] R. Lu, J. Tucker, T. Zinevitch, O. Kirichenko, V. Konoplev, K. Vitalii; S. Svetlana, J. Pickens; "Design and Synthesis of Human Immunodeficiency Virus Entry Inhibitors: Sulfonamide as an Isostere for the Ketoamide Group." *J. Med. Chem., **50(26)**, 6535-44, (2007).*

[154] M. Gonzalez, D. Gorman, C. Hamilton, G. Roth; "Process Development for the Sulfonamide Herbicide Pyroxsulam." Org. Proc. Res. Develop., ***12(2)***, 301-03, (2008).

[155] S. Claudiu, A. Innocenti and A. Scozzafava; "Antiviral sulfonamide derivatives." *Mini-Rev. Med. Chem., **4(2)**, 189-200, (2004).*

[156] W. Zhu, P. Wu, X. Liang, Y. Dong, J. Zhang; "Design, synthesis, and fungicidal activity of macrolactones and macrolactams with a sulfonamide side chain." *J. Agri. Food Chem., **56(15)**, 6547-53, (2008).*

[157] H. Chen, S. Gross, T. Dean; "2H-Thieno[3,2-e]- and [2,3-e]-1,2-thiazine-6- sulfona mide 1,1-dioxides as ocular hypotensive agents: synthesis, carbonic anhydrase inhibition and evaluation in the rabbit." *Bioorg. Med. Chem., **8(5)**, 957-975, (2000).*

[158] J. Semple, R. Edward, Y. Susan Y; "Design, Synthesis, and Evolution of a Novel, Selective and Orally Bioavailable Class of Thrombin Inhibitors: P1-Argininal Derivatives Incorporating P3-P4 Lactam Sulfonamide Moieties." *J. Med. Chem., **39(23)**, 4531-36, (1996).*

[159] M. Nair, S. Regupathy; "Studies on Cu(II)-mixed ligand complexes containing a sulfa drug and some enzyme constituents." *J. Coord. Chem., **63(2)**, 361-72, (2010)*

SYNTHESIS AND CHARACTERISATION

Synthesis of 2-amino-4-(2-chlorobenzo[h]quinolin-3-yl)-6-(4-methoxy-Phenyl) pyridine-3-carbonitrile

[A] Synthesis of N-(naphthalen-1-yl) acetamide:

A mixture of 1-naphthyl amine (0.01M) and acetic anhydride (0.01M) in methanol (LR) (20 ml) was refluxed in water bath for 2-3 hrs using CH_3COOH as catalyst. The crude product was isolated and crystallized from absolute ethanol.

[B] Synthesis of 2-chloro benzo[h]quinoline-3-carbaldehyde:

N-(naphthalen-1-yl) acetamide (0.01M) was added in a mixture of Vilsmeier-Haack reagent (prepared by drop wise addition of 6.5 ml $POCl_3$ in ice cooled 2ml DMF) and refluxed for 27 hrs. The reaction mixture was poured into ice and kept for overnight followed by neutralization using sodium bicarbonate. The crude product was isolated and crystallized from ethanol.

[C] Synthesis of 3-(2-chlorobenzo[h]quinolin-3-yl)-1-(4-methoxy-Phenyl) prop-2-en-1-one:

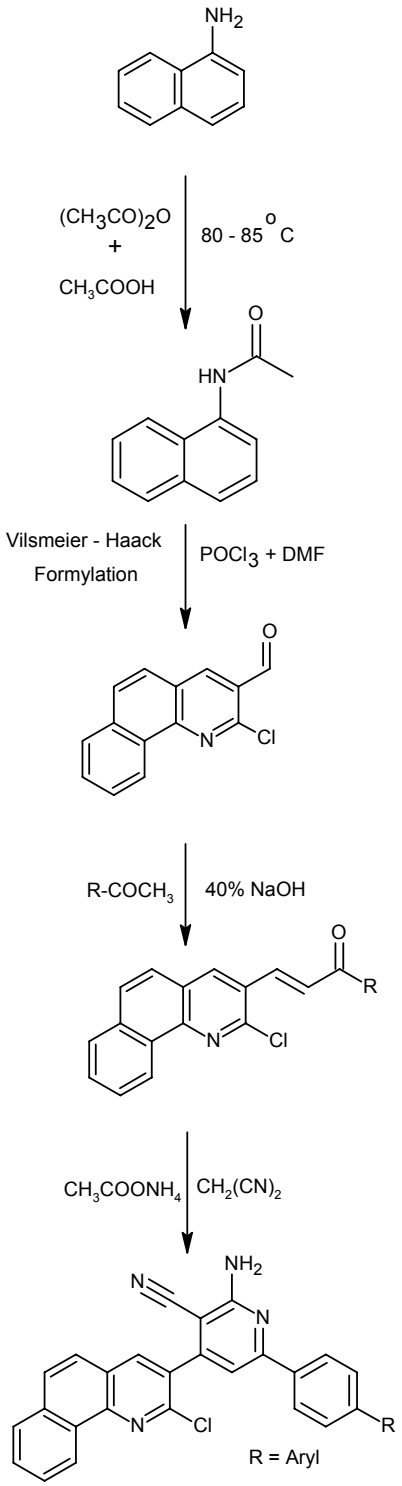
To a well stirred solution of 2-chloro benzo[h]quinoline-3-carbaldehyde (0.01M) and p-methoxy-acetophenone (0.01M) in the binary mixture of ethanol (25 ml): DMF (5ml), 40% NaOH was added till the solution became basic. The reaction mixture was stirred for 48 hrs. The contents were poured into ice, acidified, filtered and crystallized from ethanol.

[D] Synthesis of 2-amino-4-(2-chlorobenzo[h]quinolin-3-yl)-6-(4-methoxy-phenyl) pyridine-3-carbonitrile (CP-1):

A mixture of 3-(2-chlorobenzo[h]quinolin-3-yl)-1-(4-methoxy- phenyl) prop-2-en-1-one (0.01 M), malononitrile (0.01 M) and ammonium acetate (0.08 M) in ethanol (30 ml) was refluxed for 10-12 hrs. The content was poured on crushed ice. The product obtained was filtered, washed with water and crystallized from DMF.

Similarly, other substituted cyanopyridines have been prepared.

REACTION SCHEME



The characterization was done by IR, ^{1}H NMR and mass spectra.

Infrared spectra:

The IR spectra were recorded by SHIMADZU-FTIR-8400 Spectrophotometer in the frequency range of 4000-400 cm^{-1} by KBr powder method. Figure 1.1 shows IR spectra of CP-1. The IR spectral data for CP-1 is given in Table 1.2. The spectral data for all other compounds of this series are reported in Table 1.3.

^{1}H NMR Spectra:

The NMR spectra were recorded by BRUKER Spectrometer (400 MHz) using internal reference TMS and solvent $CDCl_3$/DMSO. Figure 1.2 shows NMR spectra of CP-1. The spectral data for CP-1 is given in Table 1.4.

Mass spectra:

The Mass spectra were recorded by GCMS-SHIMADZU-QP2010. Figure 1.3 shows mass spectra of CP-1.The proposed mass fragmentation of the same compound is also given in Scheme 1.1.

Figure 1.1: IR spectra of 2-amino-4-(2-chlorobenzo[h]quinolin-3-yl)-6-(4-methoxy- phenyl) pyridine-3-carbonitrile. (CP-1).

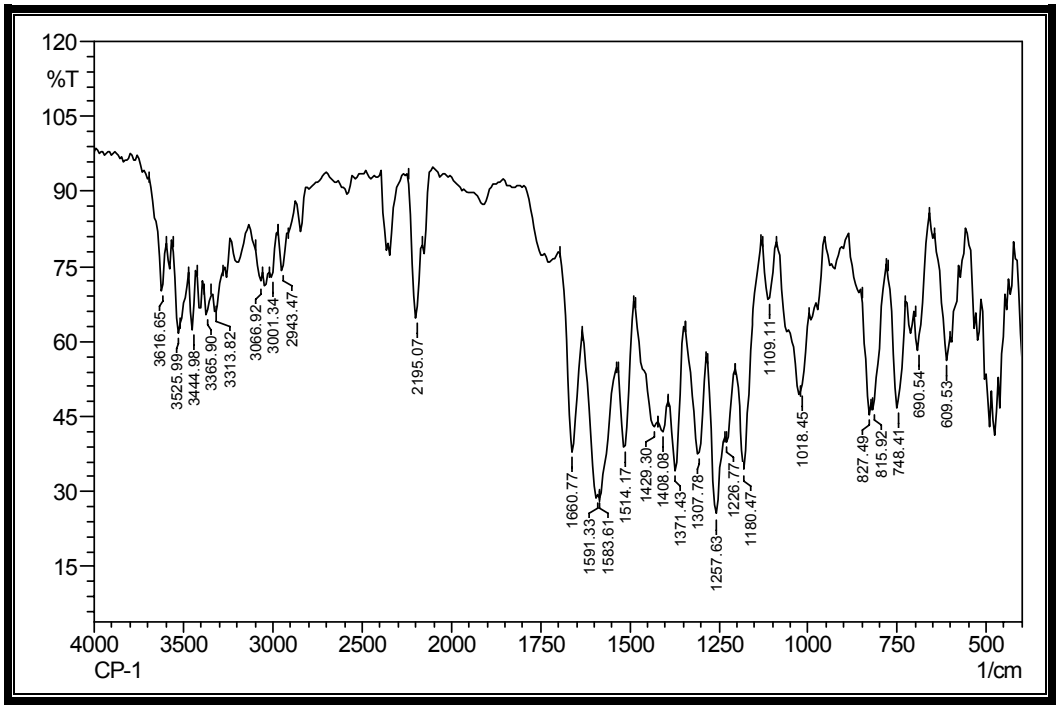


Table 1.2: IR spectral data of 2-amino-4-(2-chlorobenzo[h]quinolin-3-yl)-6-(4-methoxy- phenyl) pyridine-3-carbonitrile. (CP-1).

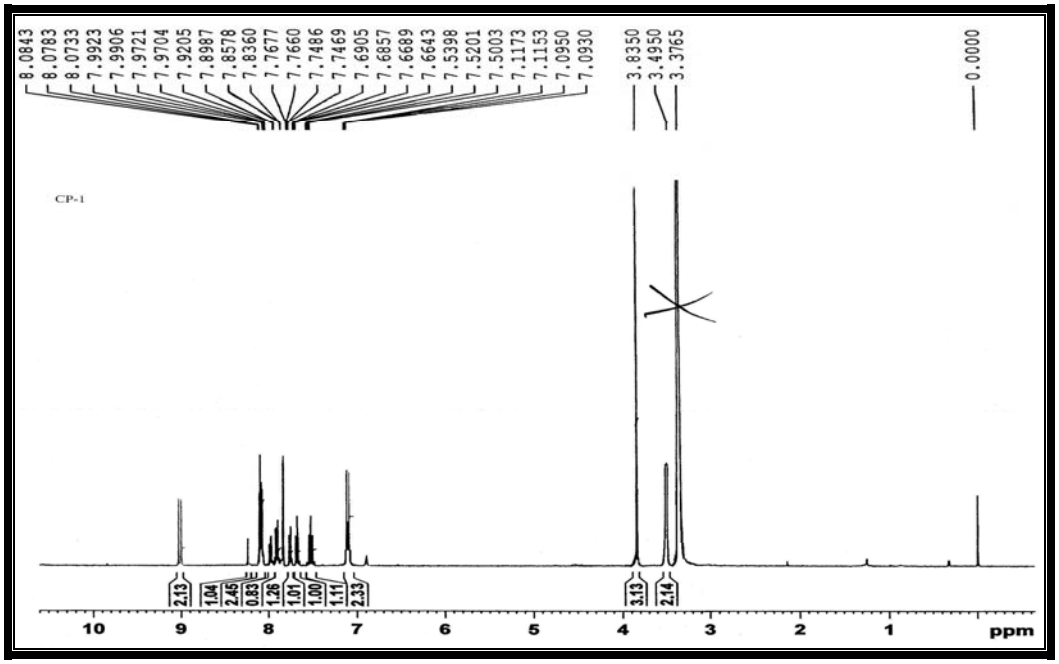
Type	Vibration mode	Frequency in cm^{-1}	
		Observed	Reported*
Alkane (methyl)	C-H str. (asym.)	2943.47	2975-2920
	C-H def. (asym.)	1429.30	1470-1435
	C-H def.(sym.)	1371.43	1395-1370
Aromatic	C-H str.	3066.92	3100-3000
	C=C str.	1514.17	1585-1480
	C-H i.p. def.	1109.11	1125-1090
	C-H o.o.p. def.	827.49	860-810
Quinoline+ pyridine ring	C=N str.	1660.77	1690-1640
	C-N str.	1257.63	1350-1200
	C≡N (Nitrile) str.	2195.07	2240-2200
ether	C-O-C str. (asym.)	1226.77	1275-1200
	C-O-C str. (sym.)	1018.45	1075-1020
	C-Cl	690.54	800-600
Amine	N-H str.	3313.82	3400-3200
	N-H def.	1591.33	1650-1590

* V. M. Parikh; "Absorption spectroscopy of organic molecule", Addition Wesley Pub. Co. London, 243-56 (1978).
* C. N. Rao; "Chemical application of Infrared Spectroscopy", Academic Press, New York (1963).

Table 1.3: IR spectral data of synthesized cyanopyridines.

Compound code	*IR ν, (cm^{-1})*				
	C=C	**C≡N**	**N-H**	**C-Cl**	**R**
CP-2	1518.33	2201.23	3347.63	698.81	2926.34
CP-3	1512.41	2198.45	3332.09	709.13	581.19
CP-4	1524.27	2212.74	3318.31	718.78	3373.54
CP-5	1503.51	2208.31	3321.26	695.42	1360.15
CP-6	1530.16	2226.78	3306.55	685.28	3318.27
CP-7	1522.09	2205.61	3319.42	698.60	729.32
CP-8	1514.70	2221.34	3311.33	712.16	1325.24
CP-9	1526.41	2207.86	3320.75	688.53	3392.83
CP-10	1521.05	2218.39	3309.22	701.37	-

Figure 1.2: ^{1}H NMR spectra of 2-amino-4-(2-chlorobenzo[h]quinolin-3-yl)-6-(4-methoxy- phenyl) pyridine-3-carbonitrile (CP-1).



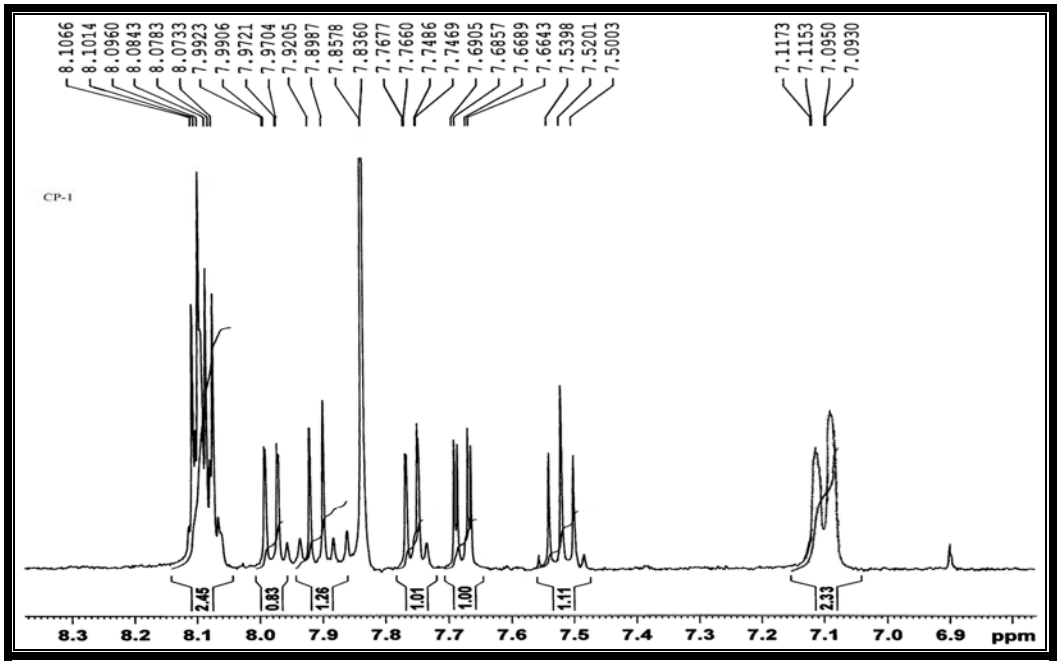
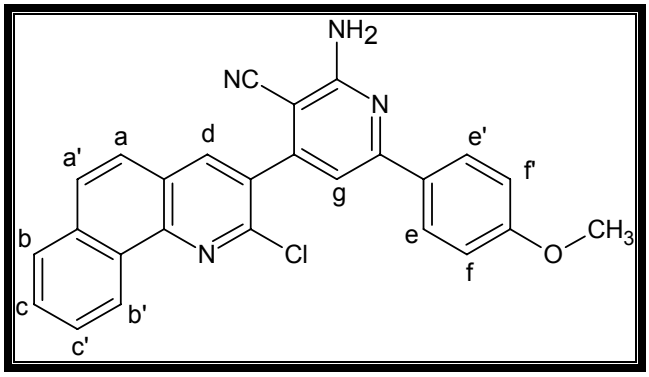


Table 1.4:^{1}H NMR spectral data of 2-amino-4-(2-chlorobenzo[h]quinolin-3-yl)-6-(4-methoxy- phenyl) pyridine-3-carbonitrile (CP-1).



Signal No.	Signal Position (δ ppm)	Relative No. of Protons	Multiplicity	Inference	*J* (Hz)
1	3.83	3	singlet	-OC<u>H</u>$_3$	-
2	3.49	2	singlet	-N<u>H</u>$_2$	-
2	7.09-7.12	2	doublet	Ar-H$_{ff'}$	8.12
3	7.50-7.54	1	triplet	Ar-H$_c$	7.92
4	7.66-7.76	2	double doublet	Ar-H$_{a'c'}$	-
5	7.83-7.99	2	multiplet	Ar-H$_{ee'}$	-
6	8.07-8.10	2	multiplet	Ar-H$_{ab}$	-
7	8.37	1	sinlet	Pyr-H$_g$	-
8	8.51	2	doublet	Ar-H$_{db'}$	7.01

SYNTHESIS AND CHARACTERISATION

Synthesis of 4-(2-chlorobenzo[h]quinolin-3-yl)-6-(4-methoxyphenyl) pyrimidin-2-amine.

[A] Synthesis of N-(naphthalen-1-yl) acetamide: Section-I [A]

[B] Synthesis of 2-chloro benzo[h]quinoline-3-carbaldehyde: Section-I [B]

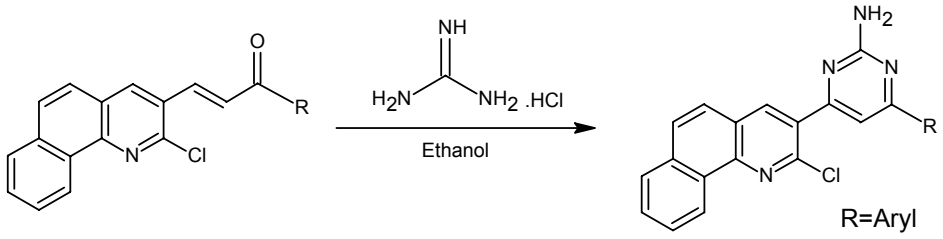
[C] Synthesis of 3-(2-chlorobenzo[h]quinolin-3-yl)-1-(4-methoxy-Phenyl) prop-2-en-1-one: Section -I [C]

[D] Synthesis of 4-(2-chlorobenzo[h]quinolin-3-yl)-6-(4-methoxyphenyl) pyrimidin-2-amine (JRM-1):

A mixture of 3-(2-chlorobenzo[h]quinolin-3-yl)-1-(4-methoxy- Phenyl) prop-2-en-1-one (0.01M) and guanidine hydrochloride (0.01M) in presence of potassium hydroxide (1 g) was refluxed in ethanol (30 ml) for 8-10 hours. The resulting mixture was poured on crushed ice. The product obtained was filtered and crystallized from DMF.

Similarly, other substituted aminopyrimidines have been prepared.

REACTION SCHEME



The physical data are reported in Table 2.1.

The characterization was done by IR, NMR and mass spectral data. The instruments used are same as mentioned in Section-I. Figures 2.1and 2.2 show the IR and NMR spectra for JRM-1, whereas Figure 2.3 shows the mass spectra for JRM-6. The IR and NMR spectral data for this compound is given in Tables 2.2 and 2.4 respectively. Table 2.3 shows the IR spectral data of all other synthesized compounds. The proposed mass fragmentation is reported in Scheme 2.1.

Figure 2.1: IR spectra of 4-(2-chlorobenzo[h]quinolin-3-yl)-6-(4-methoxy phenyl) pyrimidin-2-amine (JRM-1).

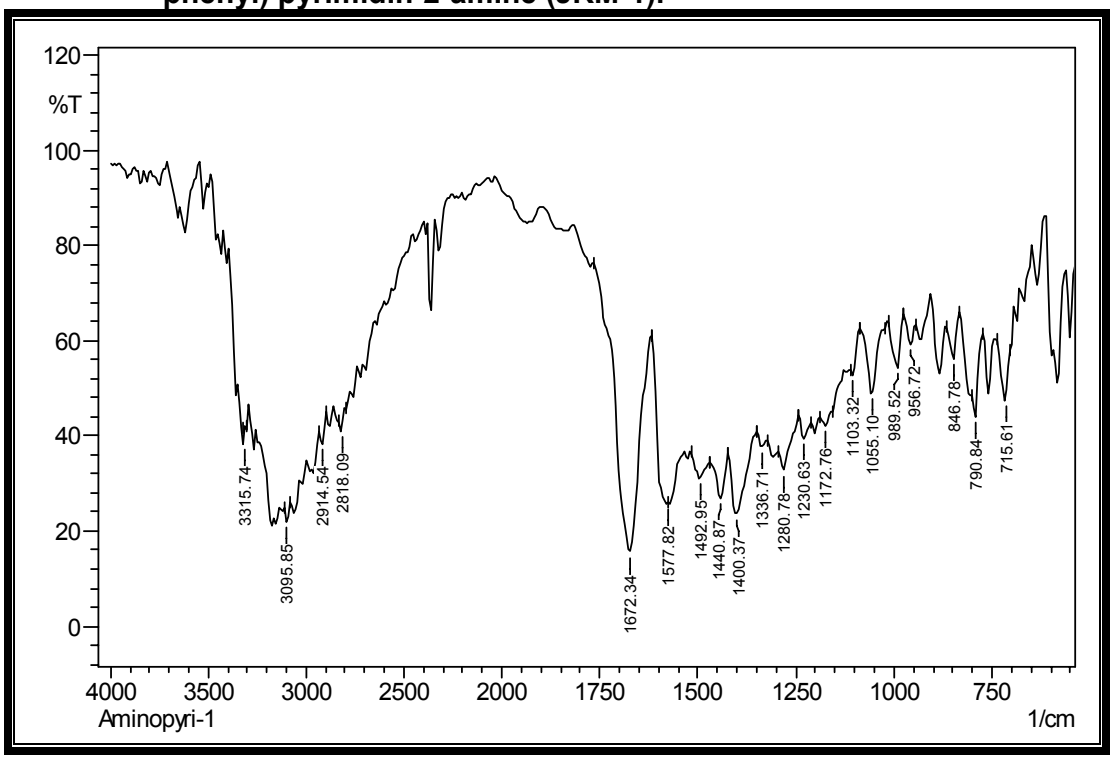


Table 2.2: IR spectral data of 4-(2-chlorobenzo[h]quinolin-3-yl)-6-(4-methoxyphenyl)pyrimidin-2-amine (JRM-1).

Type	Vibration mode	Frequency in cm^{-1}	
		Observed	Reported*
Alkane (methyl)	C-H str. (asym.)	2914.54	2975-2920
	C-H str. (sym.)	2818.09	2880-2860
	C-H def. (asym.)	1440.37	1470-1435
	C-H def.(sym.)	1336.71	1395-1370
Aromatic	C-H str.	3095.85	3100-3000
	C=C str.	1577.82	1585-1480
	C-H i.p. def.	1103.32	1125-1090
	C-H o.o.p. def.	846.78	860-810
Quinoline+ pyrimidine ring	C=N str.	1672.34	1690-1640
	C-N str.	1280.78	1350-1200
ether	C-O-C str. (asym.)	1230.63	1275-1200
	C-O-C str. (sym.)	1055.10	1075-1020
	C-Cl	790.84	800-600
Amine	N-H str.	3315.74	3400-3200
	N-H def.	1577.82	1650-1590

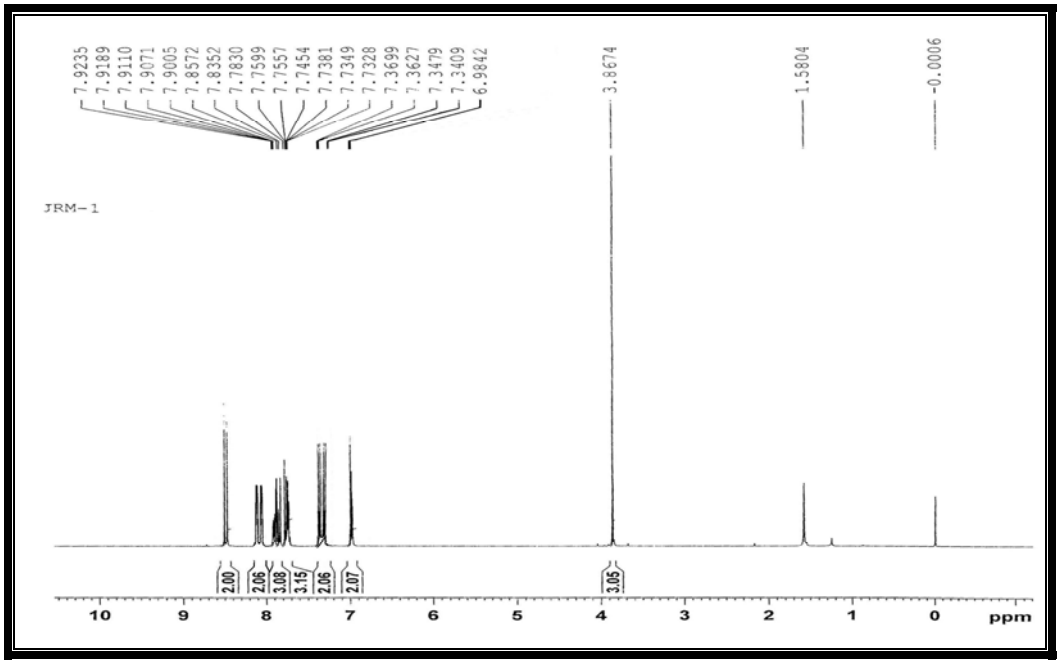
* M. Parikh; "Absorption spectroscopy of organic molecule", Addition Wesley Pub. Co. London, 243-56 (1978).

* C. N. R. Rao; "Chemical application of Infrared Spectroscopy", Academic Press, New York (1963).

Table 2.3: IR spectral data of synthesized aminopyrimidines.

Compounds	*IR ν, (cm^{-1})*				
	C=C	**C-N**	**N-H**	**C-Cl**	**R**
JRM-2	1521.42	1262.14	3308.13	741.18	2940.51
JRM-3	1560.08	1255.32	3322.54	733.40	1328.24
JRM-4	1539.11	1280.58	3331.46	751.68	3265.33
JRM-5	1520.17	1275.33	3318.33	764.09	1331.19
JRM-6	1545.51	1261.81	3307.55	755.33	3302.81
JRM-7	1560.56	1249.36	3342.16	722.52	745.72
JRM-8	1524.18	1268.65	3335.27	758.29	1328.40
JRM-9	1511.84	1245.29	3220.71	724.35	3318.57
JRM-10	1565.20	1271.72	3339.18	747.06	-

Figure 2.2: ^{1}H NMR spectra of 4-(2-chlorobenzo[h]quinolin-3-yl)-6-(4-methoxyphenyl) pyrimidin-2-amine (JRM-1).



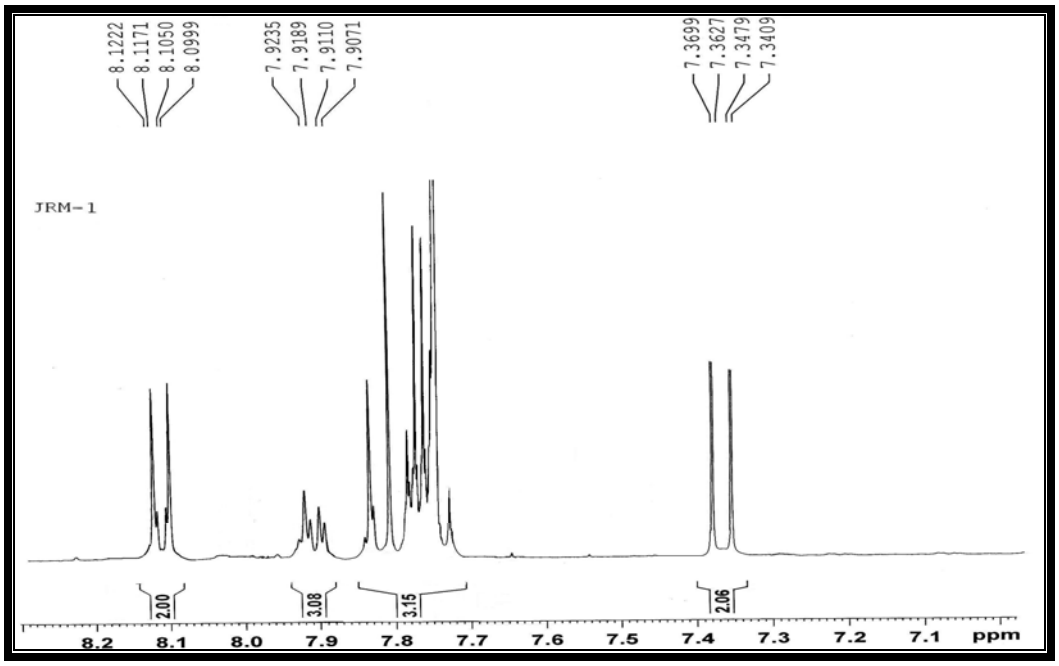
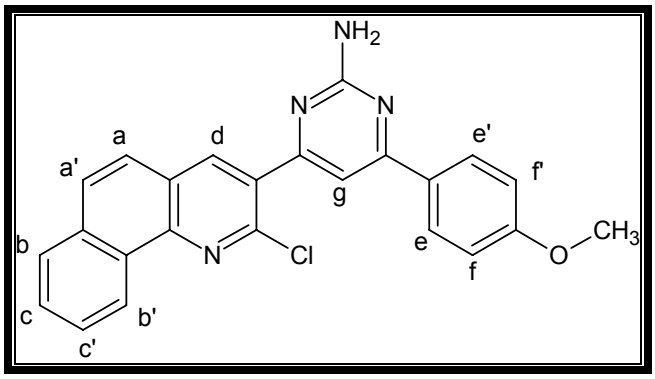


Table 2.4: ^{1}H NMR spectral data of 4-(2-chlorobenzo[h]quinolin-3-yl)-6-(4-methoxyphenyl) pyrimidin-2-amine (JRM-1).



Singal No.	Signal Position (δ ppm)	Relative No. of Protons	Multiplicity	Inference	*J* (Hz)
1	3.86	3	singlet	-OC<u>H</u>$_3$	-
2	6.98	2	singlet	-N<u>H</u>$_2$	-
2	7.34-7.37	2	doublet	Ar-H$_{ff'}$	5.92
3	7.73-7.78	3	multiplet	Ar-H$_{cc'g}$	-
4	7.90-7.92	3	multiplet	Ar-H$_{ee'a'}$	-
5	8.01-8.12	2	doublet	Ar-H$_{ab}$	4.90
6	8.51	2	doublet	Ar-H$_{db'}$	7.5

SYNTHESIS AND CHARACTERISATION

Synthesis of 2-(2-chlorobenzo[h]quinolin-3-yl)-4-(4-methoxyphenyl)-1H-1, 5-benzodiazepine.

[A] Synthesis of N-(naphthalen-1-yl) acetamide: Section-I [A]

[B] Synthesis of 2-chloro benzo[h]quinoline-3-carbaldehyde: Section-I [B]

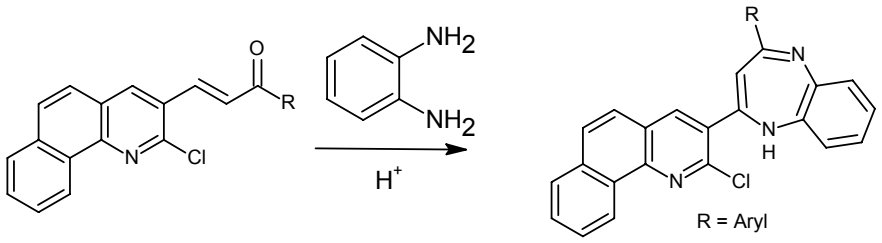
[C] Synthesis of 3-(2-chlorobenzo[h]quinolin-3-yl)-1-(4-methoxy-Phenyl) prop-2-en-1-one: Section -I [C]

[D] Synthesis of 2-(2-chlorobenzo[h]quinolin-3-yl)-4-(4-methoxyphenyl)-1H-1,5-benzodiazepine:

A mixture of 3-(2-chlorobenzo[h]quinolin-3-yl)-1-(4-methoxy Phenyl) prop-2-en-1-one, o-phenylenediamine (0.01 M) in ethanol (20ml) + DMF (5 ml) and glacial CH_3COOH (3-4 drops) was refluxed for 8-10 hrs. The resulting mixture was poured on crushed ice. The product obtained was filtered and crystallized from ethanol.

Similarly, other substituted benzodiazepines have been prepared.

REACTION SCHEME



The physical data are reported in Table 3.1.

The characterization was done by IR, NMR and mass spectral data. The instruments used are same as mentioned in Section-I. Figures 3.1, 3.2 and 3.3 show the IR, NMR and mass spectra for JRM-1. The IR and NMR spectral data for this compound is given in Tables 3.2 and 3.4 respectively. Table 3.3 shows the IR spectral data of all other synthesized compounds. The proposed mass fragmentation is reported in Scheme 3.1.

Figure 3.1: IR spectra of 2-(2-chlorobenzo[h]quinolin-3-yl)-4-(4-methoxyphenyl)-1H-1,5-benzodiazepine (MRV-1).

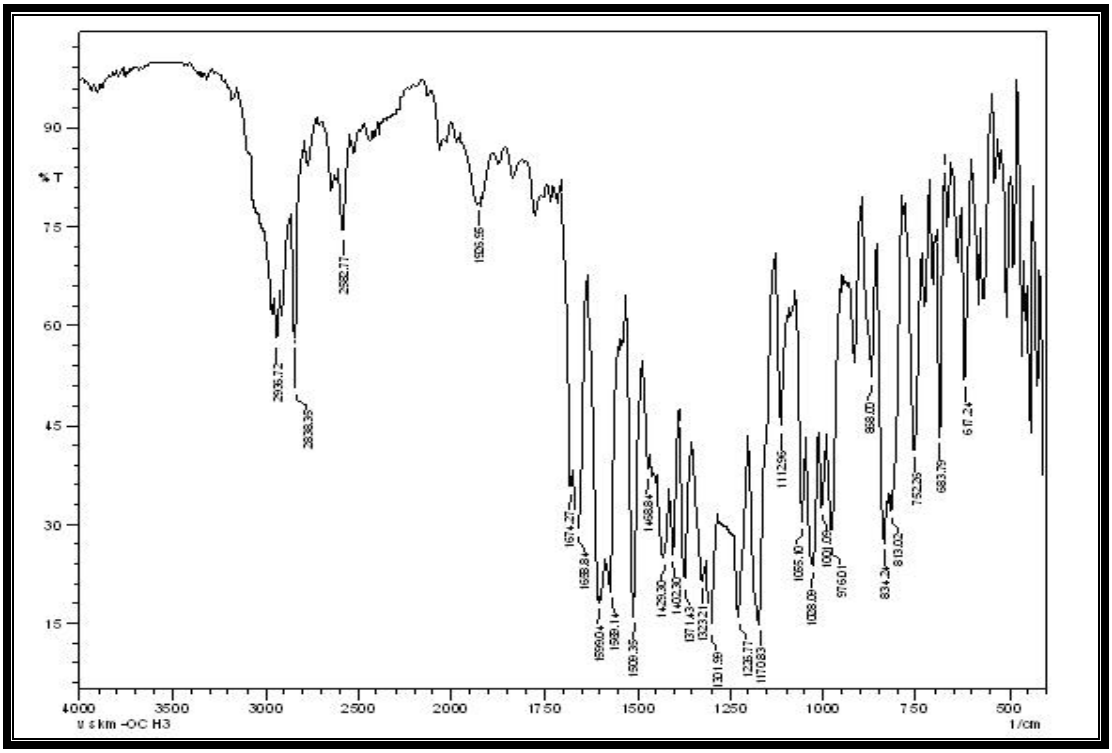


Table 3.2: IR spectral data of 2-(2-chlorobenzo[h]quinolin-3-yl)-4-(4-methoxyphenyl)-1H-1,5-benzodiazepine (MRV-1).

Type	Vibration mode	Frequency in cm^{-1}	
		Observed	Reported*
Alkane (methyl)	C-H str. (asym.)	2935.72	2975-2920
	C-H str. (sym.)	2876.35	2880-2860
	C-H def. (asym.)	1468.84	1470-1435
	C-H def.(sym.)	1371.43	1395-1370
Aromatic	C=C str.	1503.35	1585-1480
	C-H i.p. def.	1112.96	1125-1090
	C-H o.o.p. def.	834.24	860-810
Quinoline+ Diazepine ring	C=N str.	1674.27	1690-1640
	C-N str.	1301.99	1350-1200
	N-H def.	1599.04	1650-1550
ether	C-O-C str. (asym.)	1235.37	1275-1200
	C-O-C str. (sym.)	1065.10	1075-1020
	C-Cl	752.25	800-600

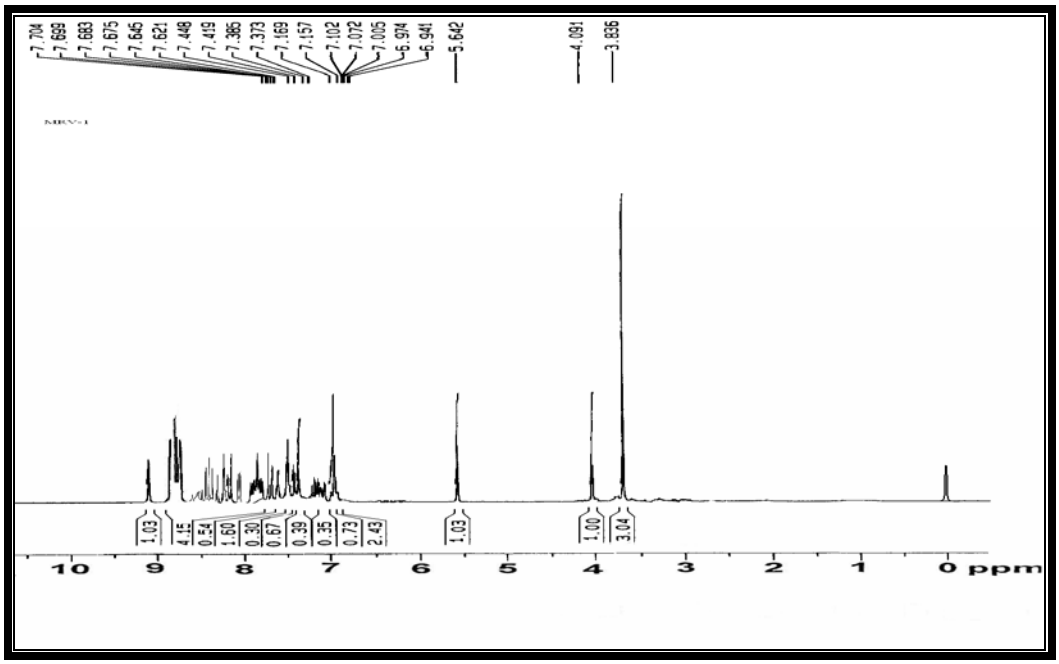
* V. M. Parikh; "Absorption spectroscopy of organic molecule", Addition Wesley Pub. Co. London, 243-56 (1978).

* C. N. R. Rao; "Chemical application of Infrared Spectroscopy", Academic Press, New York (1963).

Table 3.3: IR spectral data of synthesized benzodiazepines.

Compound code	*IR ν, (cm^{-1})*			
	C=C	**C=N**	**C-Cl**	**R**
MRV-2	1518.09	1651.33	750.32	2937.14
MRV-3	1535.40	1645.29	746.51	549.31
MRV-4	1521.18	1655.87	755.26	3271.22
MRV-5	1514.30	1665.31	740.35	1321.35
MRV-6	1537.05	1655.10	738.22	3329.40
MRV-7	1528.78	1641.43	727.50	735.45
MRV-8	1510.54	1671.65	734.54	1331.71
MRV-9	1542.66	1652.34	744.47	3316.32
MRV-10	1525.10	1659.55	725.43	-

Figure 3.2: ^{1}H NMR spectra of 2-(2-chlorobenzo[h]quinolin-3-yl)-4-(4-methoxyphenyl)-1H-1,5-benzodiazepine (MRV-1).



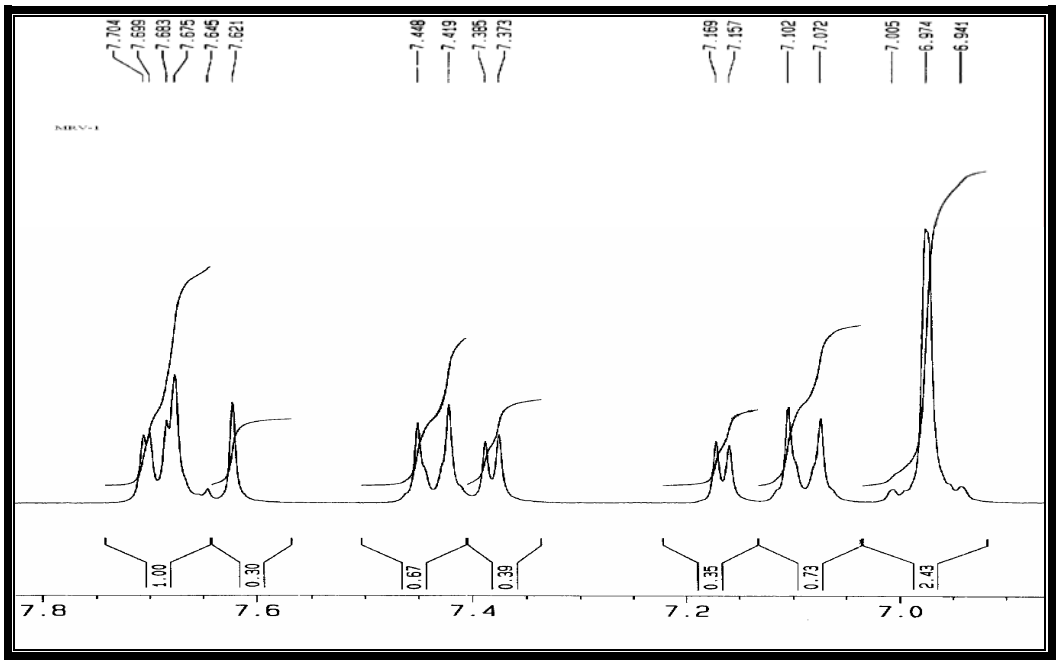
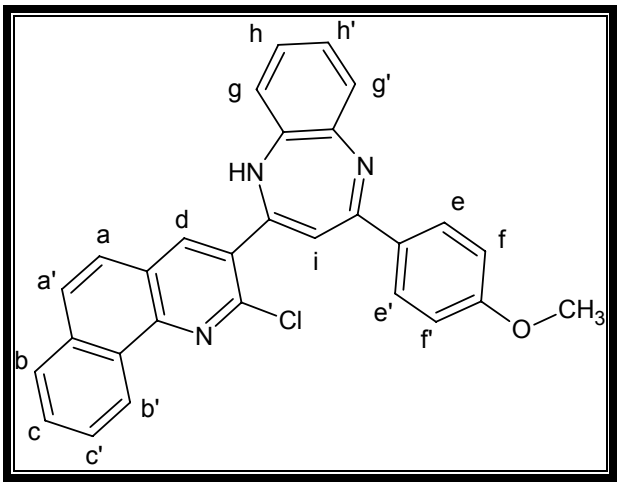


Table 3.4: ^{1}H NMR spectral data of 2-(2-chlorobenzo[h]quinolin-3-yl)-4-(4-methoxyphenyl)-1H-1,5-benzodiazepine (MRV-1).



Singal No.	Signal Position (δ ppm)	Relative No. of Protons	Multiplicity	Inference	*J* (Hz)
1	3.83	3	singlet	-OC<u>H</u>$_3$	-
2	4.09	1	singlet	N-<u>H</u>	-
3	5.64	1	singlet	H_i	
4	6.94-7.05	2	triplet	Ar-$H_{ff'}$	-
5	7.07-7.10	1	doublet	Ar-$H_{g'}$	-
6	7.15-7.16	1	doublet	Ar-$H_{h'}$	-
7	7.37-7.44	2	doublet	Ar-$H_{ee'}$	-
8	7.62-7.70	2	doublet	Ar-$H_{cc'}$	8.12
9	7.85-8.06	2	doublet	Ar-$H_{aa'}$	8.23
10	8.04-8.10	2	doublet	Ar-H_{bg}	3.51
11	9.27	1	singlet	Ar-H_d	-

SYNTHESIS AND CHARACTERISATION

Synthesis of 2-chloro-3-[3-(4-methoxyphenyl)-4, 5-dihydro-1H-pyrazol-5-yl] benzo[h] quinoline.

[A] Synthesis of N-(naphthalen-1-yl) acetamide: Section-I [A]

[B] Synthesis of 2-chloro benzo[h]quinoline-3-carbaldehyde: Section-I [B]

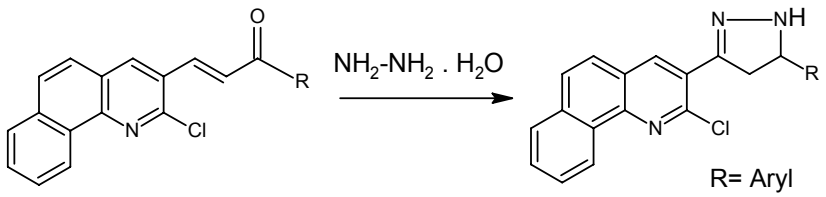
[C] Synthesis of 3-(2-chlorobenzo[h]quinolin-3-yl)-1-(4-methoxy-Phenyl) prop-2-en-1-one: Section -I [C]

[D] Synthesis of 2-chloro-3-[3-(4-methoxyphenyl)-4, 5-dihydro-1H-pyrazol -5-yl] benzo[h] quinoline (JRV-1).

A mixture of 3-(2-chlorobenzo[h]quinolin-3-yl)-1-(4-methoxy- phenyl) prop-2-en-1-one (0.01 M) and hydrazine hydrate (0.012 M) in ethanol (20 ml) was refluxed on a water bath for 6 hrs. The product was isolated and recrystallized from DMF.

Similarly, other substituted pyrazolines have been prepared.

REACTION SCHEME



The physical data are reported in Table 4.1.

The characterization was done by IR, NMR and mass spectral data. The instruments used are same as mentioned in Section-I. Figures 4.1, 4.2 and 4.3 show the IR, NMR and mass spectra for JRM-1. The IR and NMR spectral data for this compound is given in Tables 4.2 and 4.4 respectively. Table 4.3 shows the IR spectral data of all other synthesized compounds. The proposed mass fragmentation is reported in Scheme 4.1.

Figure 4.1: IR spectra of 2-chloro-3-[3-(4-methoxyphenyl)-4, 5-dihydro-1H-pyrazol -5-yl] benzo[h] quinoline (JRV-1).

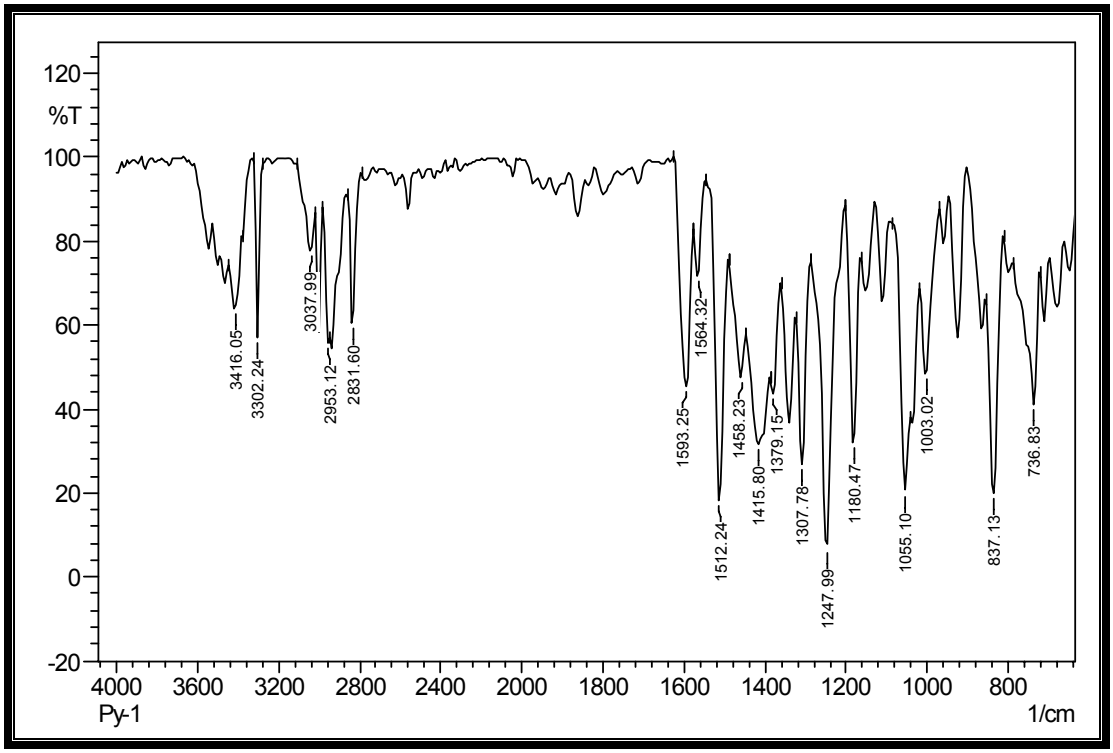


Table 4.2: IR spectral data of 2-chloro-3-[3-(4-methoxyphenyl)-4, 5-dihydro-1H-pyrazol -5-yl] benzo[h] quinoline (JRV-1).

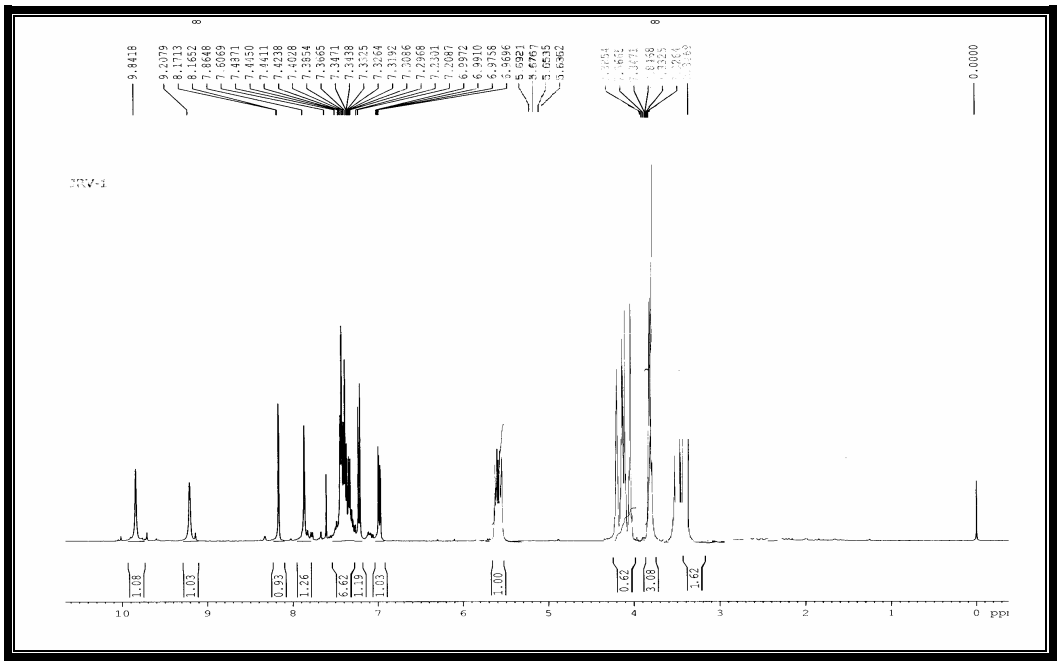
Type	Vibration mode	Frequency in cm^{-1}	
		Observed	Reported*
Alkane (methyl)	C-H str. (asym.)	2953.12	2975-2920
	C-H str. (sym.)	2831.60	2880-2860
	C-H def. (asym.)	1458.23	1470-1435
	C-H def.(sym.)	1379.15	1395-1370
Aromatic	C-H str.	3037.99	3100-3000
	C=C str.	1564.32	1585-1480
	C-H i.p. def.	1055.10	1125-1090
	C-H o.o.p. def.	837.10	860-810
Quinoline+ oxazole ring	C=N str.	1593.25	1690-1640
	C-N str.	1307.78	1350-1200
	N-O str.	843.28	850-800
ether	C-O-C str. (asym.)	1247.99	1275-1200
	C-O-C str. (sym.)	1003.02	1075-1020
	C-Cl	736.83	800-600

* V. M. Parikh; "Absorption spectroscopy of organic molecule", Addition Wesley Pub. Co. London, 243-56 (1978).
* C. N. Rao; "Chemical application of Infrared Spectroscopy", Academic Press, New York (1963).

Table 4.3: IR spectral data of synthesized pyrazolines.

Compounds	*IR ν, (cm^{-1})*				
	C=C	**C-N**	**N-O**	**C-Cl**	**R**
JRV-2	1588.31	1288.42	844.22	785.50	2928.10
JRV-3	1515.07	1261.46	855.17	704.22	571.65
JRV-4	1495.23	1299.32	822.71	696.45	3324.51
JRV-5	1521.77	1309.29	808.33	704.77	1330.24
JRV-6	1530.64	1350.55	851.60	754.89	3329.57
JRV-7	1498.50	1331.88	817.42	680.35	788.11
JRV-8	1501.85	1320.17	841.30	699.57	1308.34
JRV-9	1551.12	1308.44	825.52	775.61	3338.77
JRV-10	1491.69	1315.35	845.62	755.69	-

Figure 4.2: ^{1}H NMR spectra of 2-chloro-3-[3-(4-methoxyphenyl)-4, 5-dihydro-1H-pyrazol -5-yl] benzo[h] quinoline (JRV-1).



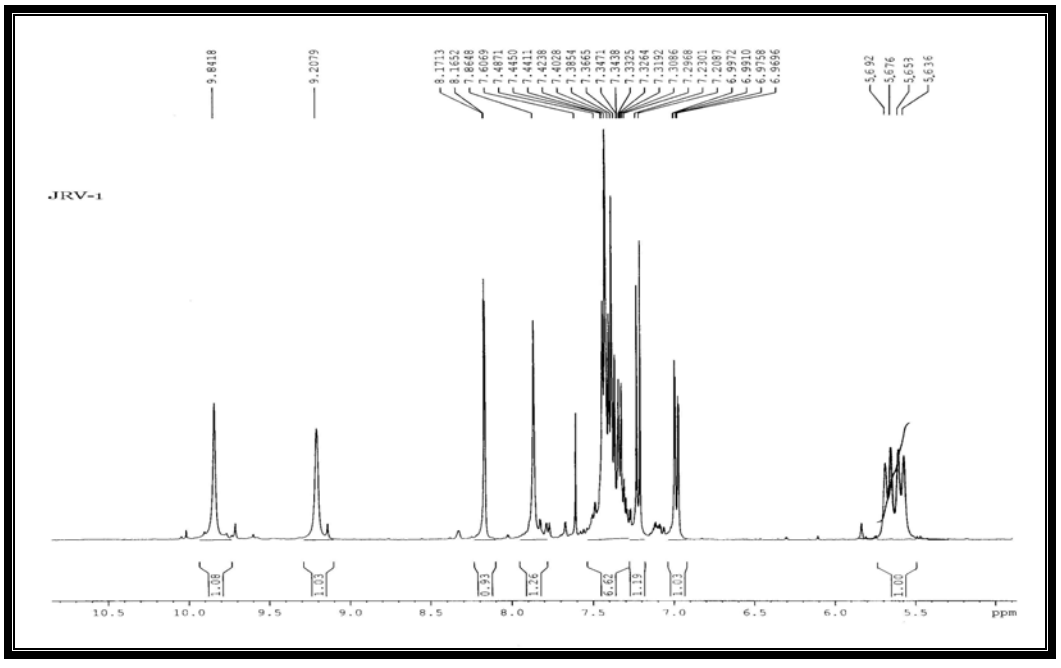
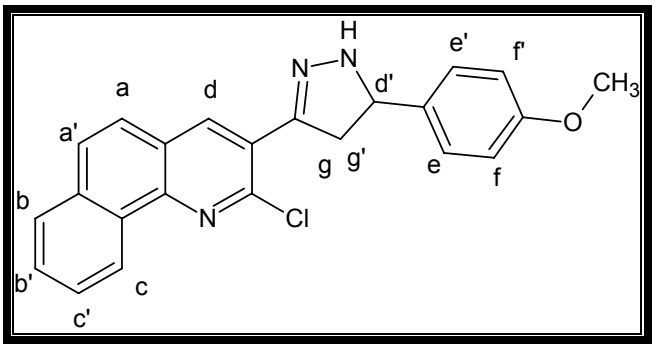


Table 4.4: ^{1}H NMR spectral data of 2-chloro-3-[3-(4-methoxyphenyl)-4, 5-dihydro-1H-pyrazol -5-yl] benzo[h] quinoline (JRV-1).



Singal No.	Signal Position (δ ppm)	Relative No. of Protons	Multiplicity	Inference	*J* (Hz)
1.	3.82	3	singlet	-OC<u>H</u>$_3$	-
2.	3.41	1	Double doublet	Pyr-Hg	7.2
3.	4.15	1	Double doublet	Pyr-Hg’	7.2
4.	6.96-6.99	1	doublet	Ar-H$_{ff'}$	8.52
5.	7.20	1	doublet	-H$_e$	-
6.	7.29-7.60	6	multiplet	Ar-H	-
7.	7.86	1	singlet	Ar-H$_c$	-
8.	9.20	1	doublet	Ar-H$_a$	7.60

SYNTHESIS AND CHARACTERISATION

Synthesis of N'-[(2-chlorobenzo[h]quinolin-3-yl)methylidene]-4-methyl benzenesulfonohydrazide .

[A] Synthesis of N-(naphthalen-1-yl) acetamide: Section-I [A]

[B] Synthesis of 2-chloro benzo[h]quinoline-3-carbaldehyde: Section-I [B]

[C] Synthesis of 2-chloro-3-[hydrazinylidenemethyl]benzo[h]quinoline:

A mixture of 2-chloro benzo[h]quinoline-3-carbaldehyde (0.012 M) in ethanol and hydrazine hydrate (0.01M) was refluxed for 2hrs. The contents were poured in crushed ice and neutralized excess hydrazine hydrate with hydrochloric acid. The product was crystallized from DMF.

[D] Preparation of 4-methyl benzene sulfonyl chloride:

It was prepared by the condensation of p- methyl benzoic acid (0.01M) with chlorosulphonic acid (0.01M) by refluxing it in water bath for 6 hours. The content was isolated and crystallized using ethanol.

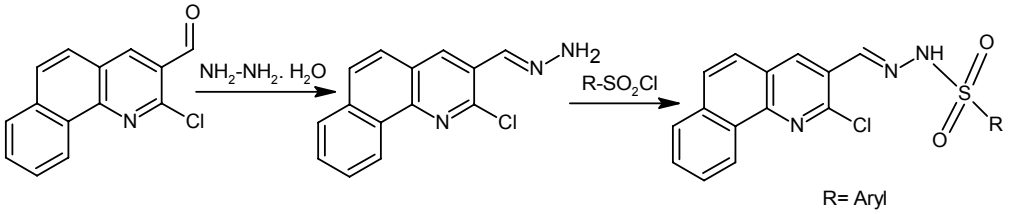
Similarly, other aryl sulphonyl chlorides were prepared.

[E] Synthesis of N'-[(2-chlorobenzo[h]quinolin-3-yl)methylidene]-4-methyl benzenesulfonohydrazide (VSM-1).

A mixture of 4-methyl benzene sulfonyl chloride (0.01M) and 2-chloro-3-[hydrazinylidenemethyl]benzo[h]quinoline (0.01M) in dry pyridine (10 ml) was refluxed on a water bath for for 5-6 hrs. The contents were poured into crushed ice and neutralized. The product was crystallized from DMF.

Similarly, other sulphonamides have been prepared.

REACTION SCHEME



The physical data are reported in Table 5.1.

The characterization was done by IR, NMR and mass spectral data. The instruments used are same as mentioned in Section-I. Figures 5.1, 5.2 and 5.3 show the IR, NMR and mass spectra for VSM-1. The IR and NMR spectral data for this compound is given in Tables 5.2 and 5.4 respectively. Table 5.3 shows the IR spectral data of all other synthesized compounds. The proposed mass fragmentation is reported in Scheme 5.1.

Figure 5.1: IR spectra of N'-[(2-chlorobenzo[h]quinolin-3-yl)methylidene]-4-methyl benzenesulfonohydrazide (VSM-1).

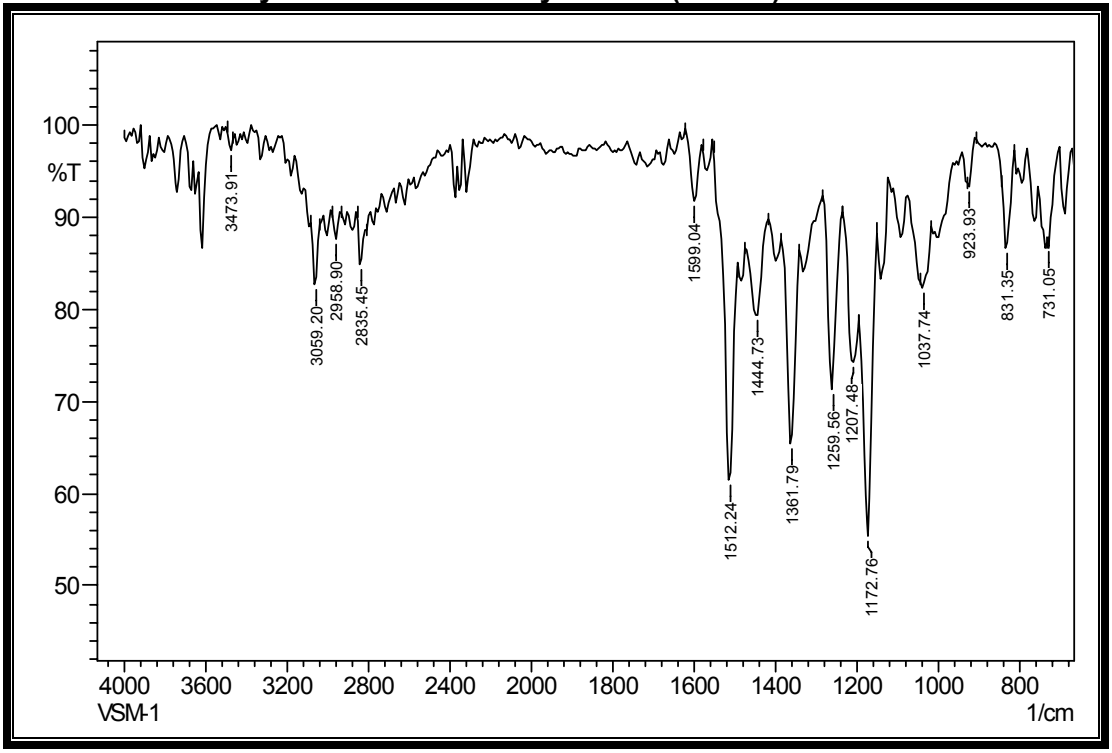


Table 5.2: IR spectral data of N'-[(2-chlorobenzo[h]quinolin-3-yl) methylidene]-4-methyl benzenesulfonohydrazide (VSM-1).

Type	Vibration mode	Frequency in cm^{-1}	
		Observed	Reported*
Alkane (methyl)	C-H str. (asym.)	2958.90	2975-2920
	C-H str. (sym.)	2835.45	2880-2860
	C-H def. (asym.)	1444.73	1470-1435
	C-H def.(sym.)	1361.79	1395-1370
Aromatic	C-H str.	3059.20	3100-3000
	C=C str.	1512.24	1585-1480
	C-H o.o.p. def.	831.35	860-810
Quinoline ring	C=N str.	1599.04	1690-1640
	C-N str.	1259.56	1350-1200
	C-Cl	725.26	800-600
Sulphonamide	N-H str.	3473.91	3450-3200
	S=O str. (asym.)	1361.76	1380-1300
	S=O str. (sym.)	1172.76	1180-1140
	N-SO_2 str.	831.35	906-828

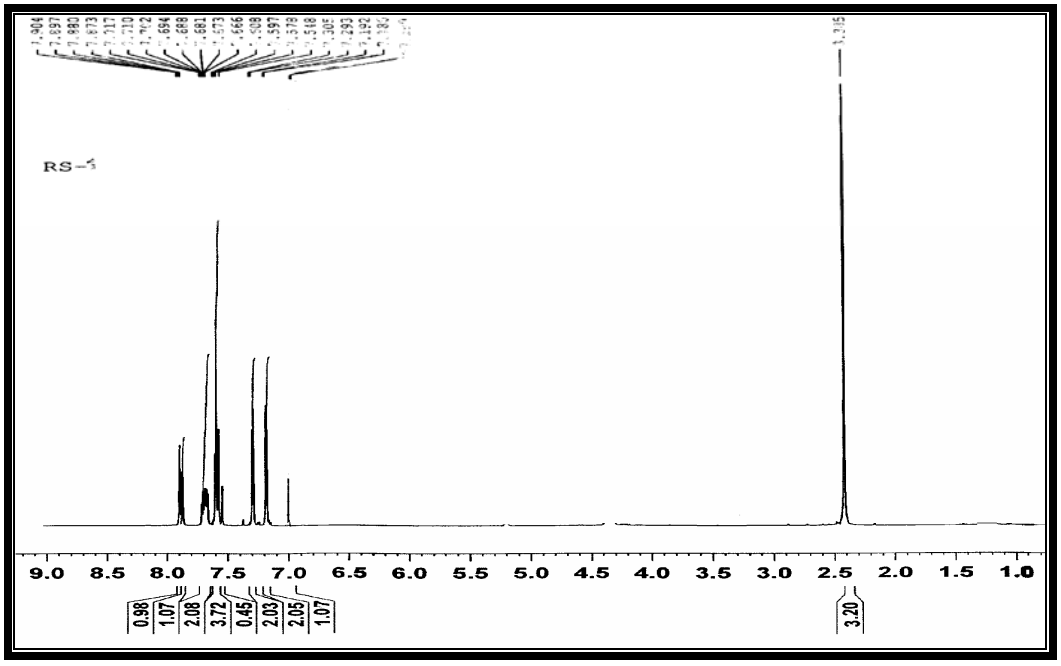
***** V. M. Parikh; "Absorption spectroscopy of organic molecule", Addition Wesley Pub. Co. London, 243-56 (1978).

* C. N. R. Rao; "Chemical application of Infrared Spectroscopy", Academic Press, New York (1963).

Table 5.3: IR spectral data of synthesized sulphonamides.

Compounds	*IR ν, (cm^{-1})*				
	C=C	**C-N**	**S=O**	**C-Cl**	**R**
VSM-2	1480.30	1311.25	1150.21	741.36	3365.58
VSM-3	1544.33	1278.51	1156.72	725.84	3374.22
VSM-4	1508.11	1247.29	1133.78	712.54	3360.43
VSM-5	1533.64	1325.54	1164.35	724.41	3355.10
VSM-6	1587.01	1300.07	1128.18	748.56	3361.54
VSM-7	1528.54	1308.98	1177.24	745.35	3370.98
VSM-8	1531.54	1333.61	1138.89	710.21	736.65
VSM-9	1514.38	1298.75	1154.63	724.32	741.37
VSM-10	1501.52	1300.07	1184.39	732.52	3359.81

Figure 5.2: ^{1}H NMR spectra of N'-[(2-chlorobenzo[h]quinolin-3-yl) methylidene]-4-methyl benzenesulfonohydrazide (VSM-1).



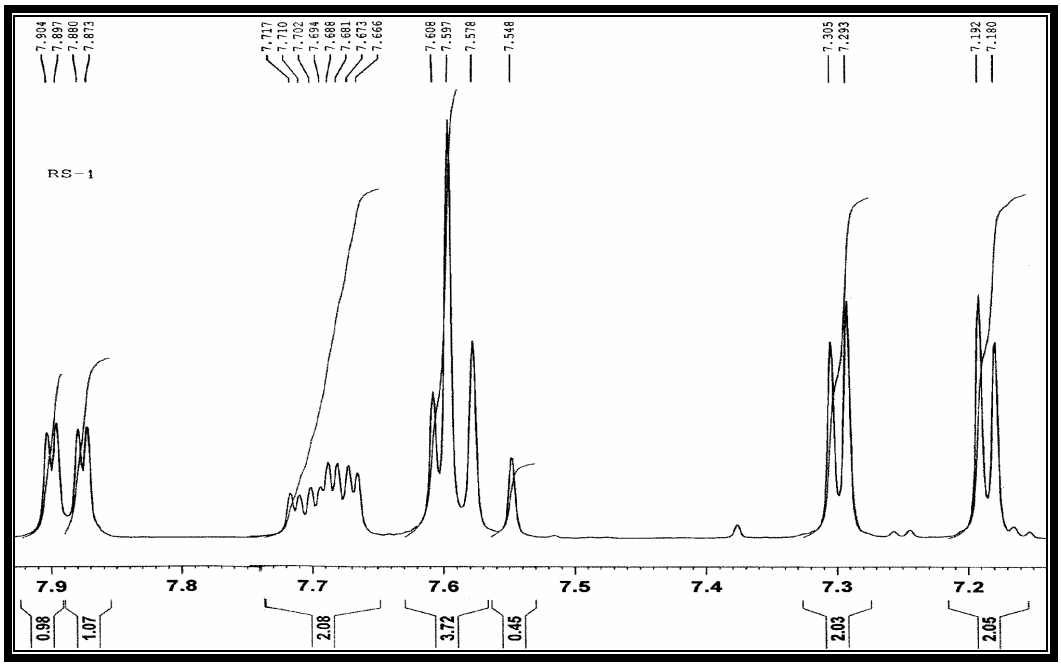
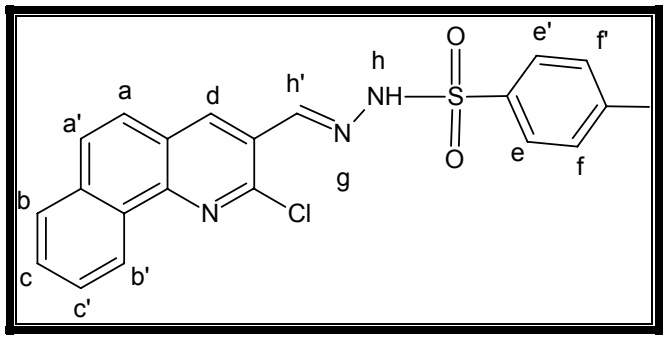


Table 5.4: ^{1}H NMR spectral data of N'-[(2-chlorobenzo[h]quinolin-3-yl) methylidene]-4-methyl benzenesulfonohydrazide (VSM-1).



Singal No.	Signal Position (δ ppm)	Relative No. of Protons	Multiplicity	Inference	*J* (Hz)
1.	3.79	3	singlet	-C<u>H</u>$_3$	-
2.	7.0	1	singlet	N-H$_h$	-
3.	7.13	1	singlet	-H$_g$	-
4.	7.18-7.19	2	doublet	Ar-H$_{ee'}$	8.52
5.	7.29-7.30	2	doublet	Ar-H$_b$	-
6.	7.54-7.71	5	multiplet	Ar-H	7.60
7.	7.90	1	singlet	N=C<u>H</u>$_{h'}$	-

INTRODUCTION

Conventional organic synthesis usually involves the heating of reactants by means of a furnace or oil bath, which heats the walls of the reaction vessel by conduction of heat. During this heating process the core of the sample takes much longer time to achieve the target temperature. To overcome such problem, the microwave assisted synthesis and sonochemical synthesis proves to be alternative options. These methods have certain benefits over conventional method such as reaction rate acceleration, milder reaction conditions, higher chemical yield, lower energy usage and different reaction selectivity.

In microwave assisted synthesis, by microwave irradiation chemical reactions[1-3] take place. Microwave heating in the laboratory was widely accepted after 1986 [4]. By microwave irradiation, target compounds are directly heated which saves time and energy.

Literature survey shows that various compounds have been synthesized by microwave assisted synthesis [5-8]. The synthesis of some other pyrazoline derivatives has also been synthesized by microwave irradiation. [9-11].

Sonochemical synthesis was first reported in 1927 by Wood and Loomis[12]. In sonochemistry, ultrasonic waves are used which interact directly with the reactants and thus reduces the reaction time. Various workers have used ultrasonic waves for the synthesis of a number of compounds. The sonochemical synthesis of some pyrazoline derivatives have also been reported[13-14].

In the present part, some substituted pyrazoline derivatives have been synthesized by using the Microwave irradiation (MW), ultrasonic irradiation (US) and by conventional (Con.) method. The comparison of these three methods is done.

EXPERIMENTAL

Methods

Conventional Thermal Synthesis:

The experimental procedure and reaction scheme for the synthesis is already given in Section-IV of Chapter-2 in experimental part.

Microwave Assisted Synthesis:

Pyrazolines have also been synthesized by microwave irradiation. Microwave-assisted procedures were carried out in a domestic QPro-M microwave oven operating at 380 W. The reactants were same as conventional method. The reactions were completed within few minutes.

Sonochemical Synthesis:

The reactants were same as above and ultrasonic irradiation was done by using Ultrasonic Interferometer (Mittal Enterprise, New Delhi, Model No. F-81) operating at a frequency of 2 MHz. All the compounds were synthesized within few hours.

RESULTS AND DISCUSSION

The reaction time and % yield of synthesized compounds by using microwave, ultrasonic waves and conventional techniques are reported in Table 1. It is observed that using microwave and ultrasonic waves, the reaction time is reduced considerably whereas % yield increased markedly.

Thus, microwave and ultrasonic waves are proved to be better techniques than conventional method.

Table 1: Comparison of % yield and reaction time of compounds synthesized by different methods.

Code	Yield %			Reaction time		
	MW	US	Con.	MW min.	US hrs.	Con. hrs.
JRV-1	76	71	59	5	3.00	7
JRV-2	71	64	52	5	3.30	7
JRV-3	73	69	61	5	2.50	8
JRV-4	79	67	55	5	3.10	7
JRV-5	71	65	59	5	3.00	9
JRV-6	69	63	58	6	3.25	8
JRV-7	73	61	55	5	3.00	8
JRV-8	81	69	57	5	3.10	7
JRV-9	70	64	58	6	3.20	8
JRV-10	76	68	60	5	3.30	9

REFERENCES

[1] C. Strauss and R. Trainor; "Developments in Microwave-assisted Organic Chemistry." *Aust. J. Chem., **48**, 1665 (1995).*

[2] H. Antonio, D. Angel Diaz, A. Moreno; "Microwaves in organic synthesis. Thermal and non-thermal microwave effects." *Chem. Soc. Rev., 164-78 (2005).*

[3] A. Loupy; "Microwaves in organic synthesis." *Wiley-VCH, Weinheim, (2006).*

[4] G. Richard, S. Frank, W. Kenneth A. Humera, B. Lorraine, L. Lena and J. Rousell; "The use of microwave ovens for rapid organic synthesis." *Tetrahedron Lett., **27(3)**, 279-82 (1986)*

[5] A. Vega, S. Cueto, A. Ramos, J. Vaquero, N. Garcia, L. Jose, B. Alvarez, A. Julio; "A microwave synthesis of the cis and trans isomers of 3-hydroxy-2-(4-methoxyphenyl)-2,3-dihydro-1,5-benzothiazepin-4(5H)-one: the influence of solvent and power output on the diastereoselectivity." *Tetrahedron Lett., **37(35)**, 6413-16 (1996).*

[6] S. Julio, M. Vazquez, M. Pilar, M. Martinez, R. Montserrat, P. Rodriguez; "Microwave enhanced synthesis of acridines. A new aspect in the Bernthsen reaction." *Green Chem., **4(4)**, 390-91(2002).*

[7] G. Martín, F. Martín, M. José, M. Carapia and B. Falcón; "Microwave-assisted synthesis of hydrated sodium uranyl oxonium silicate". *Polish J. Chem., 1399-1403 (2005).*

[8] L. Wang, D. Han, F. Xu, X. Meng, Z. Li; "Microwave assisted efficient synthesis of glucose-based 3-acetyl-5-alkyl-2,3-dihydro-1,3,4-oxadiazole derivatives catalyzed by sodium acetate." *Carbohydrate Res., **344(16)**, 2113-19 (2009).*

[9] S. Paul, R. Gupta; "Microwave assisted synthesis of 2-pyrazolines." *Ind. J. Chem., **37B(12)**, 1279-82 (1998).*

[10] S. Al-Issa, N. Andis; "Solvent-free synthesis of chalcones and N-phenyl-2-pyrazolines under microwave irradiation." *J. Saudi Chem. Soc., **9(3)**, 687-91 (2006).*

[11] K. Manna, Y. Agrawal: "Microwave assisted synthesis of new indophenazine,3,5-trisubstituted pyrazoline derivatives of benzofuran and their antimicrobial activity." *Bioorg. Med. Chem.Lett., **19(10)**, 2688-92 (2009).*

[12] R. Wood, A. Loomis; "The Physical and Biological Effects of High Frequency Sound Waves of Great Intensity." *Philos. Mag., **4**, 414 (1927).*

[13] C. Valduga, H. Braibante, M. Braibante; "Reactivity of p-phenyl substituted enamino compounds using K-10/ ultrasound. Synthesis of pyrazoles and pyrazolines." *J. Heterocyclic Chem., **35(1)**, 189- 92 (1998).*

[14] V. Pathak, R. Joshi, J. Sharma, N. Gupta, V. Rao; "Mild and ecofriendly tandem synthesis , and spectral and antimicrobial studies of N1- acetyl-5-aryl-3-(substituted styryl) pyrazoline derivatives. Phosphorus, Sulfur and Silicon and the Related Elements." ***184(7)**, 1854-65 (2009).*

INTRODUCTION

"Ultrasound" refers to the sound waves of frequency greater than the upper limit of human hearing i.e. 20 KHz (20,000 Hertz).

Due to their high frequency, human being cannot hear these sound waves. However, bats, dogs can hear these waves. Bats use ultrasounds to move in darkness and also for searching food. Dolphins and some other whales also use the ultrasounds as a hunting tool.

These ultrasound waves have various applications in various fields.In metallurgy, these ultrasonic waves are used for corrosion study and to prevent corrosion, molding and improving quality of casting[1-3], electroplating[4], thickness of galvanizing[5], surface cleaning[6], metal degreasing[7], ultrasonic welding for joining of metals[8], study of heat conduction in metals[9]. It is one of the best technique for non destructive evaluation for metals[10-13] to find out defects and cracks[14-16] for the study of alloys[17-20] and grain size measurements[21] etc.

In electronics, these waves are widely used for the determination of damage in microelectronics[22], for contaminant removal from small part of electronics[23], for cooling of integrated circuit[24], for various aspects in superconductors[25], semiconductors[26, 27], metalloids[28], insulators[29], diode[30], transistors[31], etc.

These waves are also known to be used in various industries such as cement[32-34], paper[35-36], glass[37-40], soap[41-45], petrochemicals[46-48], plastic[49-50] etc.

In engineering these waves are used for the study of various engineering properties of materials[51] such as railway tracks, cables[52, 53], etc.

In environmental science, ultrasonic waves have been used to monitor environment and environmental problems[54-57], degradation of pollutant[58, 59], waste water treatment and measurement[60-63], etc.

In the domain of medical, ultrasound waves are used for medical diagnosis[64-67], research[68-70], treatment of various diseases[71-73], in pharmaceuticals[74], etc.

In various other fields such as geosciences, geophysics[75,76], oceanography and marine science[77,78], space science, space technology and space research[79,80], nuclear technology[81-83], biology[84-86], biochemistry[87-89], bio-technology and bio-engineering[90, 91], textiles[92, 93], food, beverages and

dairy industries for healthy storage[94-99], ceramics[100,101], refractories[102,103]. nano-technology[104-106], etc. also these waves are used.

In chemistry, a wide variety of work has been done in various systems for determining various properties. These waves have also been used for the isolation, extraction, separation and filtration of organic and inorganic compounds[107-110]. Various workers studied interactions in solutions of organic and inorganic compounds[111-118], polymers[119-121], etc. A number of work has also been reported in binary[122-126], ternary[127-130] and quaternary[131] liquid mixtures. However, literature survey shows that scanty work has been done for solutions of organic compounds in different solvents. Recently, some work has been done by our research group on solutions of azomethines, triazole, sulphonamide, benzodiazepines in different solvents[132-136].

Thus, in the present chapter, acoustical properties of solutions of some cyanopyridine derivatives have been reported in DMF and DMSO solutions at 298.15 K over a wide range of concentration.

EXPERIMENTAL

The selected solvents DMF and DMSO for the present study are distilled by the reported procedure[137]. The synthesized Cyanopyridine compounds were recrystallized before use.

The densities, viscosities and ultrasonic velocities of solvents and solutions of cyanopyridine of different concentrations were measured at 298.15 K by using Pyknometer, an Ubbelohde suspended level viscometer and single frequency ultrasonic interferometer operating at 2 MHz, with the uncertainties of 0.0001 g/cm^3, $\pm$ 0.06 % and 0.01% respectively.

Density measurements:

The weight of distilled water, pure solvents and solutions of cyanopyridines were measured by using Pyknometer. The densities (ρ) were evaluated by using following equation:

$$\rho\left(g/cm^3\right) = \frac{\left(\text{wt. of solvent or solution}\right)\left(\text{density of water}\right)}{\left(\text{wt. of water}\right)} \qquad \ldots (3.1.1)$$

Viscosity Measurements:

To determine the viscosity of solution, Ubbelohde viscometer[138] was used, which obeys Stoke's law[139]. The measured quantity of the distilled water / solvent / solution was placed in the viscometer, which was suspended in a thermostat at 298.15 K. The digital stopwatch, with an accuracy of $\pm$ 0.01 sec was used to determine flow time of solutions. Using the flow times (t) and known viscosity of standard water sample, the viscosity of solvent and solutions were determined according to equation:

$$\frac{\eta_1}{\eta_2} = \frac{t_1\rho_1}{t_2\rho_2} \qquad \ldots (3.1.2)$$

where ρ_1, η_1, t_1, and ρ_2, η_2 and t_2 are the densities, viscosities and flow times of water and sample solutions, respectively.

Sound velocity measurement:

Ultrasonic interferometer, (Mittal Enterprise, New Delhi, Model No. F-81) working at frequency of 2 MHz was used to determine sound velocity.

The solvent / solution were filled in the measuring cell with quartz crystal and then micrometer was fixed. The circulation of water from the thermostat at 298.15 K was started and test solvent / solution in the cell is allowed to thermally equilibrate. The micrometer was rotated very slowly so as

to obtain a maximum or minimum of anode current (n). A number of maximum reading of anode current were counted. The total distance (d) traveled by the micrometer for n=10, was read. The wave length (λ) was determined according to the equation (3.1.3).

$$\lambda = \frac{2d}{n} \qquad \ldots (3.1.3)$$

The sound velocity (U) of solvent and solutions were calculated from the wavelength and frequency (F) according to equation (3.1.4).

$$U = \lambda F \qquad \ldots (3.1.4)$$

where frequency F is equal to 2×10^6 Hertz.

RESULTS AND DISCUSSION

Table 3.1.1 shows the experimental data of density (ρ), sound velocity (U) and viscosity (η) of synthesized Cyanopyridines (CP series) in DMF and DMSO at 298.15 K.

From these experimental data, various acoustical parameters like isentropic compressibility (κ_S), intermolecular free length (L_f), molar compressibility (W), Rao's molar sound function (R_m), Vander Waals constant (b), relaxation strength (r), apparent molar compressibility (ϕ_k) etc., were evaluated using the following equations:

1. Isentropic compressibility:

Isentropic compressibility (κ_s) can be evaluated by the equation [140]:

$$\kappa_s = \frac{1}{U^2 \rho} \qquad \ldots (3.1.5)$$

2. Intermolecular free path length:

The intermolecular free path length (L_f) was calculated by the equation given by Jacobson [141].

$$L_f = K_j \kappa_s^{1/2} \qquad \ldots (3.1.6)$$

where K_J is Jacobson constant (=2.0965 X 10^{-6})

3. Molar compressibility:

Molar compressibility (W) can be calculated by the following equation[142]:

$$W = \left(\frac{M}{\rho}\right) \kappa_s^{-1/7} \qquad \ldots (3.1.7)$$

The apparent molecular weight (M) of the solution can be calculated according to equation (3.1.8):

$$M = M_1 W_1 + M_2 W_2 \qquad \ldots (3.1.8)$$

where W_1 and W_2 are weight fractions of solvent and compound, respectively. M_1 and M_2 are the molecular weights of the solvent and compounds respectively.

Table 3.1.1: Sound Velocities, Densities and velocities of cyanopyridines In DMF and DMSO solutions at T = 298.15 K.

Conc. M	Density ρ $g.cm^{-3}$	Velocity U. 10^{-5} $cm.s^{-1}$	Viscosity η.10^{3} poise	Density ρ $g.cm^{-3}$	Velocity U. 10^{-5} $cm.s^{-1}$	Viscosity η.10^{3} poise
	DMF			***DMSO***		
	CP-1			***CP -1***		
0.00	0.9439	1.4616	7.7846	1.0959	1.4860	12.0640
0.01	0.9447	1.4632	7.9614	1.0965	1.4868	12.3761
0.02	0.9455	1.4640	8.1278	1.0967	1.4880	12.5648
0.04	0.9463	1.4652	8.2713	1.0975	1.4900	12.9006
0.06	0.9474	1.4672	8.4643	1.0982	1.4924	13.2233
0.08	0.9529	1.4696	8.8012	1.1003	1.4948	13.5625
0.10	0.9587	1.4732	9.0865	1.1033	1.4980	14.0796
	CP -2			***CP -2***		
0.01	0.9455	1.4676	7.8486	1.0961	1.4880	12.6168
0.02	0.9467	1.4700	8.0185	1.0964	1.4904	12.9613
0.04	0.9483	1.4716	8.2941	1.097	1.4928	13.2899
0.06	0.9507	1.4736	8.5820	1.0979	1.4964	13.9493
0.08	0.9549	1.4756	8.8945	1.0993	1.5056	15.1157
0.10	0.9598	1.4776	9.2214	1.1021	1.5192	17.0481
	CP -3			***CP -3***		
0.01	0.9488	1.4660	8.0118	1.0975	1.4876	12.3689
0.02	0.9528	1.4676	8.1842	1.0989	1.4896	12.7634
0.04	0.9593	1.4684	8.3849	1.1002	1.4928	13.2166
0.06	0.9615	1.4700	8.5547	1.1028	1.4972	13.9992
0.08	0.9629	1.4728	8.7309	1.1069	1.5048	14.9367
0.10	0.9691	1.4740	8.9509	1.1132	1.5164	16.3654
	CP -4			***CP -4***		
0.01	0.9471	1.4684	7.8619	1.096	1.4904	12.8425
0.02	0.9482	1.4716	8.2253	1.0962	1.4928	13.3366
0.04	0.9497	1.4732	8.5783	1.0967	1.4964	14.1929
0.06	0.9513	1.4756	8.8343	1.0975	1.5016	14.9707
0.08	0.9532	1.4788	9.1655	1.0989	1.5116	16.3101
0.10	0.9551	1.4828	9.4017	1.1018	1.5268	18.3944
	CP -5			***CP -5***		
0.01	0.9445	1.4632	7.9840	1.0965	1.4884	13.2164
0.02	0.9454	1.4636	8.2825	1.0972	1.4904	13.6593
0.04	0.9467	1.4644	8.4813	1.0979	1.4936	14.6629
0.06	0.948	1.4652	8.8811	1.099	1.4984	15.8444
0.08	0.9542	1.4660	9.2296	1.1008	1.5044	17.0551
0.10	0.9609	1.4676	9.6921	1.1043	1.5120	19.5295

Conc. M	Density ρ	Velocity U. 10^{-5}	Viscosity η.10^{3}	Density ρ	Velocity U. 10^{-5}	Viscosity η.10^{3}

	$g.cm^{-3}$	$cm.s^{-1}$	poise	$g.cm^{-3}$	$cm.s^{-1}$	poise
	DMF			***DMSO***		
	CP -6			***CP -6***		
0.00	0.9439	1.4616	7.7846	1.0959	1.4860	12.0640
0.01	0.9451	1.4804	8.0536	1.0963	1.4916	12.9037
0.02	0.9468	1.4820	8.3276	1.0965	1.4944	13.4188
0.04	0.9491	1.4832	8.5856	1.0969	1.4980	14.2814
0.06	0.9518	1.4844	8.8496	1.0974	1.5028	15.2136
0.08	0.9552	1.4860	9.1484	1.098	1.5120	16.5375
0.10	0.9585	1.4872	9.4856	1.0988	1.5276	18.5828
	CP -7			***CP -7***		
0.01	0.9461	1.4700	8.3415	1.0967	1.4900	12.6470
0.02	0.9489	1.4712	8.4808	1.0971	1.4924	13.0542
0.04	0.9522	1.4724	8.6328	1.0979	1.4956	13.9002
0.06	0.9559	1.4736	8.7894	1.0998	1.5004	14.8212
0.08	0.9601	1.4760	8.9558	1.1021	1.5084	15.9322
0.10	0.9652	1.4796	9.1362	1.1062	1.5204	17.8713
	CP -8			***CP -8***		
0.01	0.9448	1.4628	7.9157	1.0965	1.4896	12.4031
0.02	0.9458	1.4624	8.0934	1.097	1.4916	12.8149
0.04	0.9471	1.4620	8.2528	1.0976	1.4932	13.5329
0.06	0.9489	1.4628	8.3874	1.0995	1.4956	14.5096
0.08	0.9614	1.4632	8.6539	1.1019	1.4992	15.6286
0.10	0.9646	1.4640	8.8294	1.1056	1.5048	17.2729
	CP -9			***CP -9***		
0.01	0.9458	1.4844	8.0468	1.0964	1.4928	13.0042
0.02	0.9474	1.4864	8.3180	1.0967	1.4956	13.2642
0.04	0.9499	1.4876	8.6003	1.0972	1.5000	13.9060
0.06	0.9524	1.4888	8.8850	1.0979	1.5044	14.7772
0.08	0.9561	1.4896	9.1581	1.0986	1.5128	16.3106
0.10	0.9596	1.4904	9.4836	1.0999	1.5308	18.5780
	CP -10			***CP -10***		
0.01	0.9451	1.4664	7.9584	1.0966	1.4916	12.7882
0.02	0.9468	1.4676	8.0903	1.0969	1.4944	13.0212
0.04	0.9491	1.4680	8.2395	1.0975	1.4968	13.5084
0.06	0.9516	1.4684	8.3996	1.0982	1.5000	14.4274
0.08	0.9567	1.4696	8.5912	1.0991	1.5048	15.5729
0.10	0.9612	1.4712	8.7596	1.1009	1.5116	17.1404

4. Rao's molar sound function:

Rao's molar sound function (R_m) can be evaluated by an equation given by Bagchi et al. [143]:

$$R_m = \left(\frac{M}{\rho}\right) U^{1/3} \qquad \ldots (3.1.9)$$

5. Van der Waals Constant:

Van der Waals constant (b) can be calculated as follows [144]:

$$b = \frac{M}{\rho}\left\{1-\left(\frac{RT}{MU^2}\right)\left[\sqrt{1+\frac{MU^2}{3RT}}-1\right]\right\} \qquad \ldots (3.1.10)$$

where R is the gas constant (=8.3143 JK^{-1} mol^{-1}) and T is the absolute temperature.

6. Relaxation Strength:

The relaxation strength (r) can be calculated as follows [145]:

$$r = 1-\left[\frac{U}{U_\infty}\right]^2 \qquad \cdots (3.1.11)$$

where U_∞ = 1.6 x 10^5 $cm.s^{-1}$.

7. Solvation number:

$$S_n = \frac{M_2}{M_1}\left[\frac{1-\kappa_s}{\kappa_{s1}}\right]\left[\frac{100-X}{X}\right] \qquad \cdots (3.1.12)$$

where X is the number of grams of solute in 100 gm of the solution. M_1 and M_2 are the molecular weights and κ_{S1} and κ_S are isentropic compressibility of solvent and solute respectively.

8. Apparent Molar Compressibility (ϕ_k):

The apparent molar compressibility (ϕ_K) of the solutions was calculated by the following equation:

$$\phi_K = \frac{\left(\rho_0\kappa_s - \rho\kappa_s^0\right)1000}{c\rho_0} + \frac{\kappa_s^0 M_2}{\rho_0} \qquad \ldots (3.1.13)$$

where ρ_0 and κ_s^0 are density and isentropic compressibility of pure solvent respectively, c is the concentration of the solution.

Some of these calculated parameters are given in Table 3.1.2 for the studied compounds in DMF and DMSO. Figure 3.1.1 shows the variation of ultrasound velocity (*U*) with concentration in DMF and DMSO. It is observed that overall ultrasonic velocity (*U*) increases with concentration for all the compounds in both the solvents (except CP-5 in DMF). The velocity depends on intermolecular free length (L_f). The velocity increases with decrease in L_f or vice versa. It is evident from Table 3.1.2 that L_f decreases continuously, which suggests that there is strong interaction between solvent and compound molecules.

The variation of isentropic compressibility (κ_s) with concentration is shown in Figure 3.1.2 where κ_s values are found to decrease with concentration for all the compounds. Similarly, relaxation strength (*r*) (as reported in Table 3.1.2) is also observed to decrease with concentration for all the compounds. The decrease in adiabatic compressibility and relaxation strength is attributed to the fact that the cyanopyridines molecules in solutions are considerably ionized and these ions are surrounded by a layer of solvent molecules firmly bound and oriented toward the ions. The orientation of solvent molecules around the ions is attributed to the influence of the electrostatic field of the ions, which lowers the compressibility of the cyanopyridine solutions. In DMF solutions of CP-5, the decrease of ultrasonic velocity (U) and increase in relaxation strength after 0.02 concentration suggests that in CP-5, which contains p-nitro substituent, solute-solute interactions dominate at higher concentrations.

Figure 3.1.3 shows the linear variation of molar compressibility (*W*) with concentration. Further, Table 3.1.2 shows the increase of molar sound function (R_m) and Vander Waals constant (*b*) with concentration. The correlation coefficients for these parameters are in the range of 0.9991-0.9999. This linear increase of these parameters suggests the absence of complex formation in these systems.

Table 3.1.2: Some acoustical parameters of Cyanopyridine derivatives in DMF and DMSO at T = 298.15 K.

	DMF				DMSO			
Conc. M	L_f A^o	r	$R_m.10^{-3}$ $cm^{-8/3}.s^{-1/3}$	b $cm^3.mol^{-1}$	L_f A^o	r	$R_m.10^{-3}$ $cm^{-8/3}.s^{-1/3}$	b $cm^3.mol^{-1}$
	CP-1				CP -1			
0.00	1.4764	0.1655	4.0789	77.4323	1.3477	0.1374	3.7762	71.2914
0.01	1.4742	0.1637	4.1703	79.1396	1.3466	0.1365	3.8435	72.5502
0.02	1.4727	0.1628	4.2608	80.8411	1.3454	0.1351	3.9126	73.8340
0.04	1.4709	0.1614	4.4445	84.3037	1.3431	0.1328	4.0488	76.3690
0.06	1.4680	0.1591	4.6269	87.7233	1.3405	0.1300	4.1854	78.9045
0.08	1.4614	0.1564	4.7834	90.6414	1.3371	0.1272	4.3157	81.3167
0.10	1.4534	0.1522	4.9357	93.4522	1.3324	0.1234	4.4417	83.6313
	CP -2				CP -2			
0.01	1.4691	0.1587	4.1635	78.9311	1.3458	0.1351	3.8405	72.4735
0.02	1.4658	0.1559	4.2462	80.4546	1.3434	0.1323	3.9048	73.6478
0.04	1.4637	0.1541	4.4164	83.6489	1.3409	0.1295	4.0313	75.9925
0.06	1.4605	0.1518	4.5813	86.7332	1.3371	0.1253	4.1575	78.3087
0.08	1.4498	0.1490	4.6926	88.7919	1.3281	0.1145	4.2867	80.5762
0.10	1.4467	0.1471	4.8496	91.7304	1.3145	0.0984	4.4135	82.7117
	CP -3				CP -3			
0.01	1.4682	0.1605	4.1789	79.2515	1.3453	0.1356	3.8588	72.8258
0.02	1.4635	0.1587	4.2785	81.1101	1.3426	0.1332	3.9422	74.3650
0.04	1.4577	0.1577	4.4777	84.8726	1.3389	0.1295	4.1131	77.5337
0.06	1.4545	0.1559	4.6962	88.9805	1.3334	0.1244	4.2789	80.5807
0.08	1.4506	0.1527	4.9189	93.1416	1.3242	0.1155	4.4397	83.4674
0.10	1.4448	0.1513	5.1077	96.6905	1.3104	0.1018	4.5918	86.1073
	CP -4				CP -4			
0.01	1.4671	0.1577	4.1575	78.8035	1.3437	0.1323	3.8433	72.4866
0.02	1.4630	0.1541	4.2416	80.3393	1.3414	0.1295	3.9083	73.6744
0.04	1.4603	0.1522	4.4077	83.4552	1.3378	0.1253	4.0371	76.0400
0.06	1.4567	0.1495	4.5732	86.5409	1.3327	0.1192	4.1660	78.3779
0.08	1.4521	0.1458	4.7369	89.5731	1.3231	0.1074	4.2968	80.6595
0.10	1.4467	0.1411	4.9003	92.5806	1.3082	0.0894	4.4256	82.8003
	CP -5				CP -5			
0.01	1.4743	0.1637	4.1785	79.2936	1.3477	0.1346	3.8503	72.6511
0.02	1.4732	0.1632	4.2753	81.1232	1.3452	0.1323	3.9236	74.0007
0.04	1.4714	0.1623	4.4704	84.8099	1.3429	0.1286	4.0718	76.7420
0.06	1.4696	0.1614	4.6645	88.4761	1.3396	0.1230	4.2197	79.4442
0.08	1.4640	0.1605	4.8285	91.5716	1.3347	0.1159	4.3653	82.0762
0.10	1.4573	0.1587	4.9859	94.5212	1.3282	0.1070	4.5038	84.5389

Conc. M	DMF L_f A^o	DMF r	DMF $R_m.10^{-3}$ $cm^{-8/3}.s^{-1/3}$	DMF b $cm^3.mol^{-1}$	DMSO L_f A^o	DMSO r	DMSO $R_m.10^{-3}$ $cm^{-8/3}.s^{-1/3}$	DMSO b $cm^3.mol^{-1}$
			CP -6				**CP -6**	
0.00	1.4764	0.1655	4.0789	77.4323	1.3477	0.1374	3.8436	71.2914
0.01	1.4567	0.1439	4.1783	78.9824	1.3424	0.1309	3.9093	72.4728
0.02	1.4538	0.1421	4.2591	80.4801	1.3397	0.1276	4.0391	73.6663
0.04	1.4509	0.1407	4.4225	83.5462	1.3363	0.1234	4.1696	76.0507
0.06	1.4477	0.1393	4.5823	86.5413	1.3317	0.1178	4.3038	78.4238
0.08	1.4435	0.1374	4.7367	89.4262	1.3233	0.1070	4.4435	80.7843
0.10	1.4399	0.1360	4.8892	92.2793	1.3093	0.0885	3.8436	83.1222
			CP -7				**CP -7**	
0.01	1.4663	0.1559	4.1733	79.0739	1.3436	0.1328	3.8477	72.5766
0.02	1.4629	0.1545	4.2575	80.6461	1.3412	0.1300	3.9192	73.8859
0.04	1.4592	0.1531	4.4331	83.9509	1.3378	0.1262	4.0607	76.4986
0.06	1.4552	0.1518	4.6042	87.1671	1.3324	0.1206	4.1988	79.0165
0.08	1.4496	0.1490	4.7711	90.2770	1.3239	0.1112	4.3376	81.4832
0.10	1.4423	0.1448	4.9309	93.2262	1.3111	0.0970	4.4712	83.7707
			CP -8				**CP -8**	
0.01	1.4745	0.1641	4.1767	79.2678	1.3441	0.1332	3.8513	72.6511
0.02	1.4741	0.1646	4.2722	81.0873	1.3420	0.1309	3.9253	74.0147
0.04	1.4735	0.1651	4.4659	84.7709	1.3402	0.1290	4.0726	76.7645
0.06	1.4713	0.1641	4.6569	88.3814	1.3368	0.1262	4.2149	79.4043
0.08	1.4613	0.1637	4.7834	90.7745	1.3322	0.1220	4.3553	81.9831
0.10	1.4581	0.1628	4.9590	94.0881	1.3250	0.1155	4.4905	84.4233
			CP -9				**CP -9**	
0.01	1.4523	0.1393	4.1789	78.9227	1.3412	0.1295	3.8442	72.4661
0.02	1.4491	0.1370	4.2605	80.4271	1.3386	0.1262	3.9096	73.6524
0.04	1.4460	0.1356	4.4229	83.4704	1.3343	0.1211	4.0397	76.0286
0.06	1.4429	0.1342	4.5836	86.4807	1.3300	0.1159	4.1690	78.3848
0.08	1.4394	0.1332	4.7355	89.3298	1.3222	0.1060	4.3019	80.7349
0.10	1.4360	0.1323	4.8861	92.1551	1.3059	0.0846	4.4416	83.0271
			CP -10				**CP -10**	
0.01	1.4706	0.1600	4.1580	78.8471	1.3422	0.1309	3.8372	72.3529
0.02	1.4681	0.1587	4.2310	80.2106	1.3395	0.1276	3.8973	73.4391
0.04	1.4659	0.1582	4.3791	83.0099	1.3370	0.1248	4.0145	75.6080
0.06	1.4636	0.1577	4.5246	85.7612	1.3337	0.1211	4.1319	77.7645
0.08	1.4585	0.1564	4.6551	88.2100	1.3289	0.1155	4.2499	79.8992
0.10	1.4535	0.1545	4.7865	90.6678	1.3219	0.1074	4.3656	81.9508

Figure 3.1.1: Variation of ultrasonic velocity (*U*) of Cyanopyridines (CP) with concentration in [A] DMF and [B] DMSO at T=298.15 K.

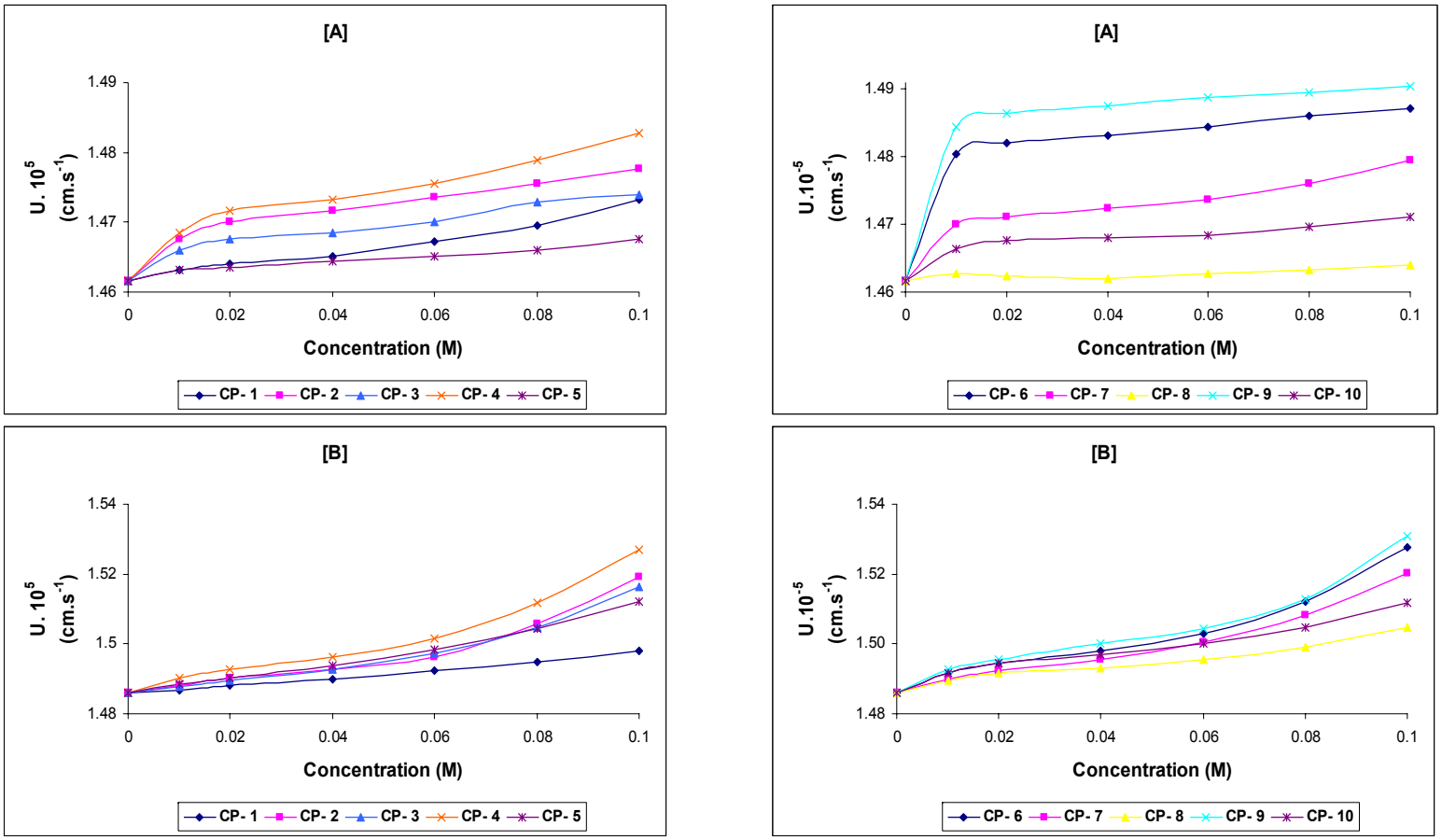


Figure 3.1.2: Variation of Isentropic compressibility (κ_s) of Cyanopyridines (CP) with concentration in [A] DMF and [B] DMSO at T=298.15 K.

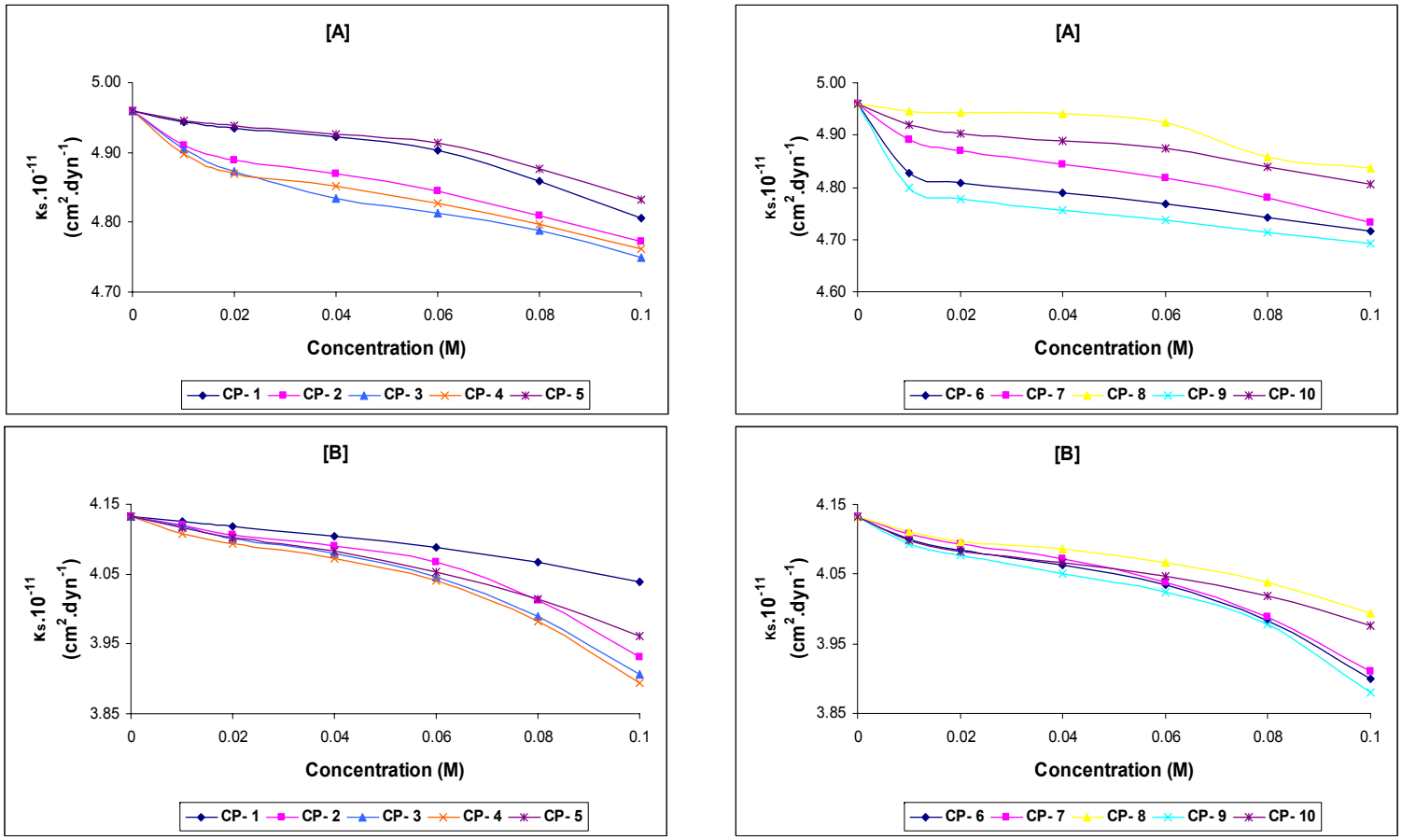


Figure 3.1.3: Variation of Molar compressibility (*W*) of Cyanopyridines (CP) with concentration in [A] DMF and [B] DMSO at T=298.15 K.

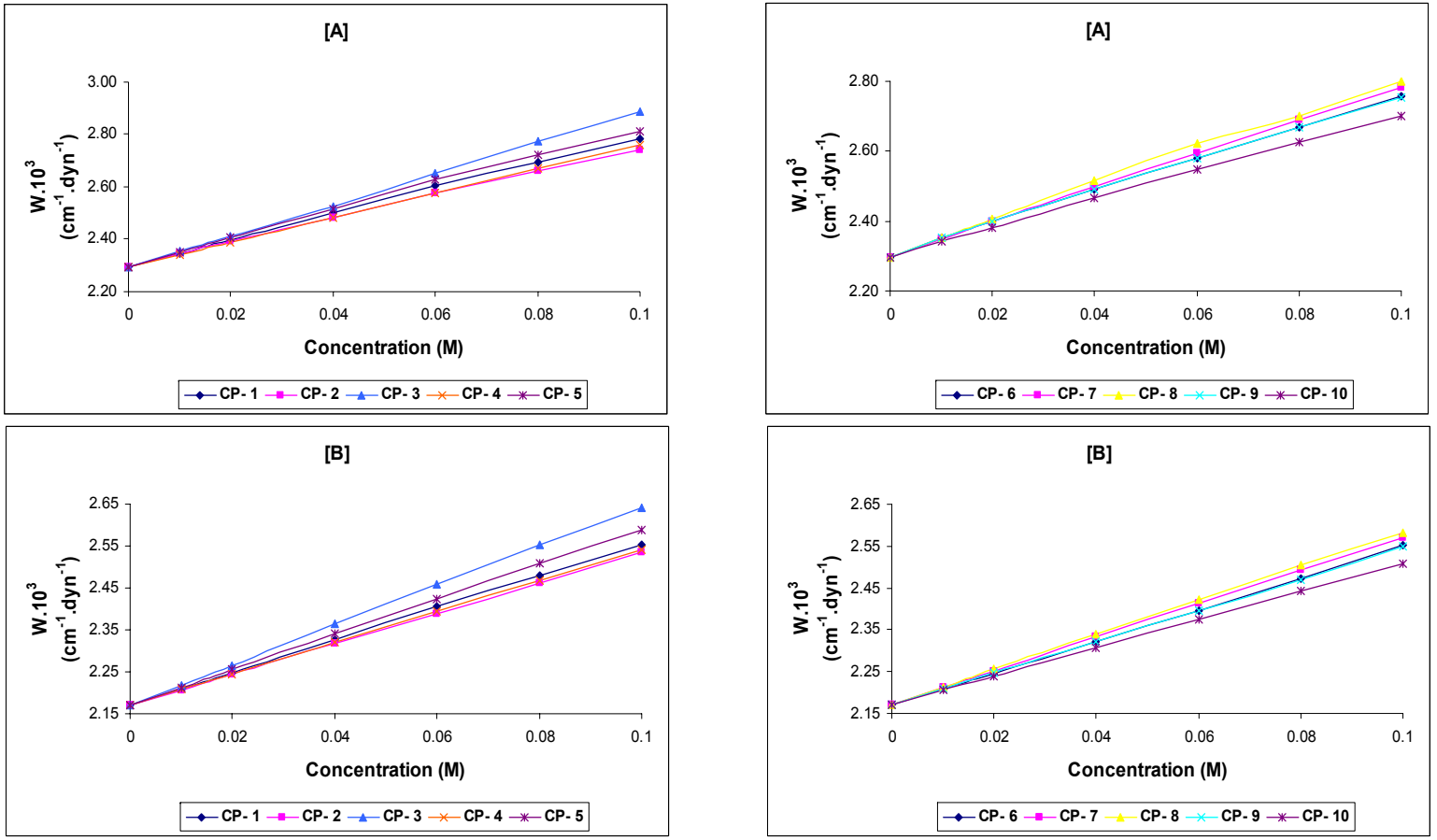


Figure 3.1.4 shows the variation of solvation number (S_n) with concentration which is found to be positive for all the systems. The solvation number is a measure of structure forming or structure breaking tendency. The positive S_n values are due to structure forming tendency of compounds in the studied solvents. Thus, the studied compounds exhibit solute-solvent interactions in both the solvents. However, comparison of solvation number in the two solvents shows that in DMF, structure forming tendency is much higher than that in DMSO. Further, in DMSO, This indicates that in DMSO, considerable amount of solute- solute interactions also exist.

The isentropic compressibility of all the solutions was also fitted to the following Bachem's relation [(146)]:

$$\kappa_s = \kappa_s^0 + AC + BC^{3/2} \qquad \ldots (3.1.14)$$

where *A* and *B* are constants, *C* is the molar concentration of solutions, and κ_S and κ_S° are the adiabatic compressibilities of the solution and solvent respectively. The constants *A* and *B* have been determined from the intercept and slope of the plots of $\left(\kappa_s - \kappa_s^0\right)/C$ verses $C^{1/2}$.

Further, apparent molar compressibility and apparent molar volume of solutions are fitted to Gucker's[(147)] and Masson's[(148)] relations:

$$\phi_k = \phi^\circ_k + S_k C^{1/2} \qquad \ldots (3.1.15)$$

$$\phi_v = \phi^\circ_v + S_v C^{1/2} \qquad \ldots (3.1.16)$$

where ϕ°_k and ϕ°_v are limiting apparent molar compressibility and limiting apparent molar volume, respectively. S_K and S_v are solute- solvent interaction parameters. The slope and intercept of plot of ϕ_k versus $C^{1/2}$ gives S_K and ϕ°_k whereas S_v and ϕ°_v are evaluated from the slope and intercept of plot of ϕ_v versus $C^{1/2}$ and values are given in Table 3.1.3.

Figure 3.1.4: Variation of Solvation Number (S_n) of Cyanopyridines (CP) with concentration in [A] DMF and [B] DMSO at T= 298.15 K.

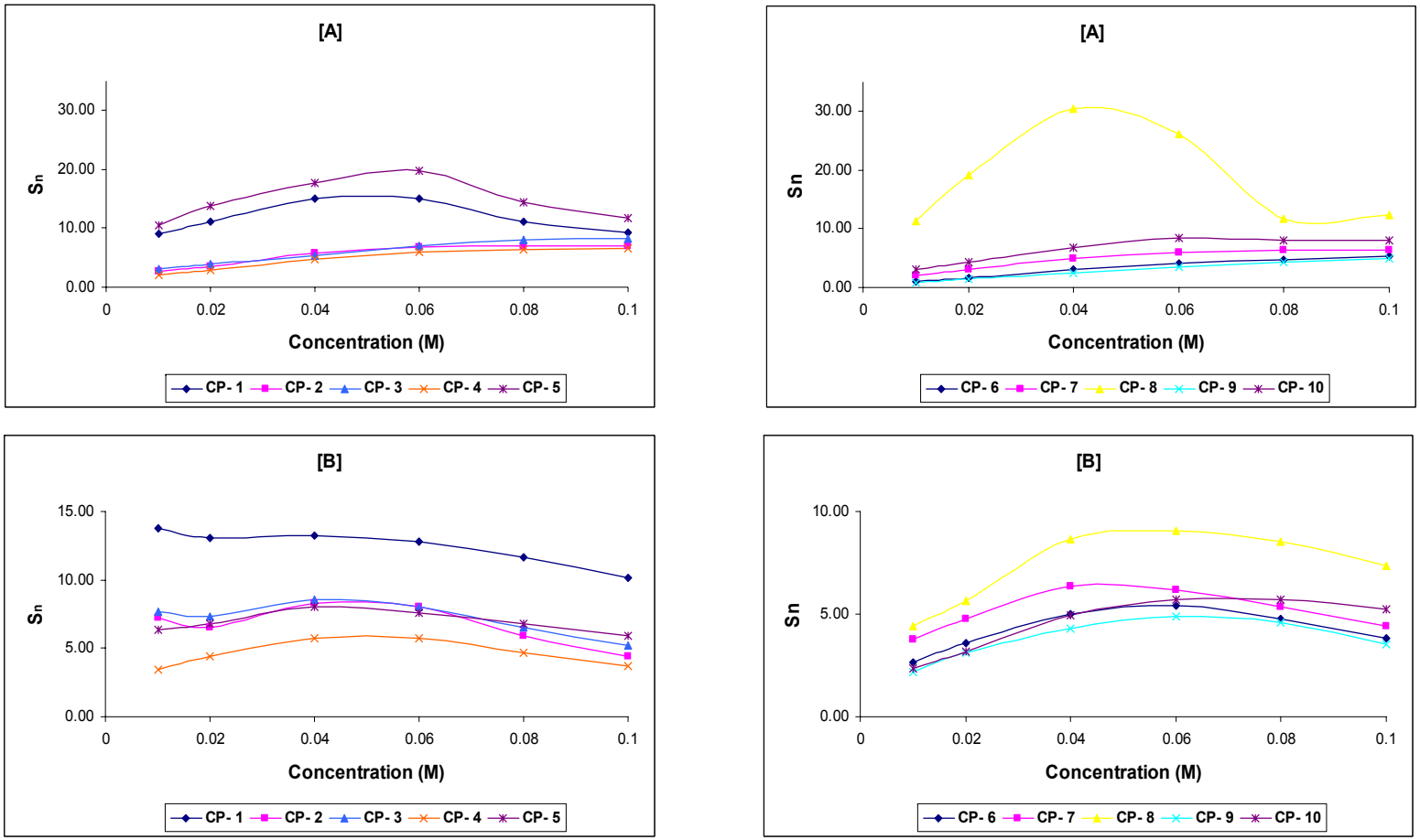


Table 3.1.3: Bachem's, Gucker's and Masson's constants of Cyanopyridines in DMF and DMSO at 298.15 K.

Comp.	A x 10^{11} dyn^{-1} cm^{-3} $.mol^{-1}$		B x 10^{11} dyn^{-1} $cm^{-1/2}$ $.mol^{-3/2}$		$\phi°_K$ x10^8 dyn^{-1} $.mol^{-1}$		S_K x 10^8 dyn^{-1} $cm^{-3/2}$ $.mol^{-3/2}$		$\phi°_v$ $cm^3.mol^{-1}$		S_v $cm^3.mol^{-1}$	
	DMF	**DMSO**	**DMF**	**DMSO**	**DMF**	**DMSO**	**DMF**	**DMSO**	**DMF**	**DMSO**	**DMF**	**DMSO**
CP-1	-2.0689	-0.6018	5.7807	-0.6332	-0.0847	0.9600	5.0287	0.6701	-15.493	25.058	748.04	334.21
CP -2	-7.5476	-1.3757	27.399	1.2916	-5.756	-0.4518	24.874	4.4506	-91.203	55.352	1658.5	-148.84
CP -3	-7.0976	-1.3526	18.52	-0.8861	-7.9125	-1.2129	25.837	6.4859	-467.41	-93.938	3988.2	1807.8
CP -4	-9.6435	-2.9966	35.182	6.6308	-8.7746	-1.7871	35.161	9.1544	-92.868	65.591	721.71	-219.89
CP -5	-1.7568	-1.7205	4.3109	1.8973	-0.0078	-0.4785	6.3363	3.6792	-4.916	50.06	365.07	370.9
CP -6	-7.2037	-4.185	15.55	11.2200	-10.328	-3.2636	34.086	15.383	-80.168	46.425	521.86	122.32
CP -7	-3.8088	-3.0619	5.268	6.8136	-7.4688	-2.2043	25.285	11.057	-149.65	-6.2484	312.75	979.05
CP -8	-1.9907	-2.9352	7.7745	8.0287	-0.1706	-1.8717	8.3544	11.319	-17.792	10.85	347.76	675.82
CP -9	-8.936	-5.1247	20.344	14.463	-7.4034	-3.7554	19.942	14.9	-129.9	35.378	1204.9	200.6
CP -10	-4.5772	-4.5495	13.262	13.523	-3.894	-3.3417	16.809	14.316	-82.502	25.686	595.94	253.23

It is observed that for all the compounds in both the solvents, A values are negative whereas B values are mostly positive. The negative A and positive B again confirms the predominance of solute-solvent interactions in the system. In DMSO, for CP-1 and CP-3, negative B again confirms the existence of solute-solute interactions in these systems. For DMF, negative ϕ°_{k} and ϕ°_{v} values are due to solute-solvent interactions. However, in DMSO, ϕ°_{k} values are negative (except CP- 1) whereas ϕ°_{v} values are mostly positive. This again confirms that in DMSO both solute-solute and solute-solvent interactions exist. This is further supported by S_K and S_v values. In DMF, both S_k and S_v values are positive and are higher than that in DMSO. Whereas for CP- 2 and CP- 4, S_v values are negative.

Thus, it is concluded that although in both the solvents, solute- solvent interactions dominate, in DMSO solute- solute interactions also exist in considerable amount which is reflected in S_n, S_K and S_v values.

REFERENCES

[1] P. Merz; "Methods of improving the quality of castings." *Sulzer Tech. Rev., **48(3)**, 161-7 (1966).*

[2] J. Mazurek, Z. Pawlowski, W. Tondys; "Ultrasonic testing of platinum and platinum-rhodium forgings and castings." "*Conf. Proc. - Int. Conf. Nondestr. Test., 7th, **2,** 617-23 (1977).*

[3] B. Cao, H. Wang, C. Jen, K. Nguyen, J. Legoux, C. Loong, M. Viens; "Ultrasonic monitoring of injection molding and die casting." *Proc. SPIE- Int. Soc.Optical Eng. 173-86 (1996).*

[4] C. Kenahan, D. Schlain; "Effects of ultrasonics on brass plating." *Tech.Proc. Am. Elec. Soc., **51(96-103)**, 103-4 (1964).*

[5] D. Van C. Edwards, S. Dixon, S. Palmer, J. Reed, C. Mason, R. Etchells, M. Harding, H. Luling, R. Cramer; "A new ultrasound system for measurement of in-situ galvanizing kettles." *Eur. Gen. Galva. Asso.Edited Proc. Int. Galva. Conf. 18th, 13/1-13/4 (1997).*

[6] Y. Tanaka, M. Ido, Y. Umeki, S. Honda; "Plastic deformation on metal surface induced by ultrasonic hammering." *Bul. of the Japan Soc. of Prec. Eng., **9(4),** 99-104 (1975).*

[7] P. Merz; "Methods of improving the quality of castings." *Sul. Tech. Rev., **48(3)**, 161-7 (1966).*

[8] P. Basak, B. Saxena, B. Das; "Nonfusion joining of aluminum." *Rec. Dev. Non-Ferro. Metals Tech., Pap. Dis. Symp., **1,** 159-68 (1969).*

[9] W. Williams, H. Fairbanks; "Influence of ultrasonics on heat conduction in metals." *Proc. of the West Virg. Aca. of Sci., **42**, 179-81 (1971).*

[10] M. Atkins, M. Druce; "Ultrasonic probe system for the continuous inspection of hot steel." *J. Iron and Steel Ins., **204(6)**, 607-8 (1966).*

[11] M. Mikhovski, L. Merkulov, A. Mechkov, S. Iordakiev; "Application possibilities of ultrasonic methods for nondestructive testing of powder metallurgic Mater. prepared on an iron powder base." Bulg. *Conf. Proc. Int. Conf. Nondestr. Test., 7th, **2,** 585-8 (1977).*

[12] R. Murayama, K. Fujisawa, M. Hirao, H. Fukuoka; "Non-destructive evaluation of formability of zinc-coated steel sheets using electromagnetic acoustic transducer." *NDT&E Int., **30(6),** 377-82 (1997).*

[13] L. Cosgriff, B. Lerch, M. Hebsur, G. Baaklini, Y. George, L. Ghosn; "Ultrasonic spectroscopy of stainless steel sandwich panels." J. *Int. SAMPE Tech. Conf., **35,** 638-52 (2003).*

[14] T. Fuji, Y. Otsuka, K. Ishihara; "Acoustic emission at the fatigue test of model spherical tank." *Adv. Weld. Tech. Int. Sym. Jpn. Weld. Soc., Proc., 2nd, 611-15 (1975).*

[15] A. Nozue, T. Kishi; "An acoustic emission study of the intergranular cracking of AISI 4340 steel." *J. Acou. Emis.,* ***1(1)****, 1-6 (1982).*

[16] D. Nelson, H. Yuce, L. Chow; "A study of the growth of small fatigue cracks in a high strength steel using a surface acoustic wave technique." *Fatigue & Frac. Eng. Mater. & Str.,* ***17(11),*** *1357-69 (1994).*

[17] J. Holt, I. Palmer, D. Goddard; "The interpretation of acoustic emission signals from the deformation of low alloy steels." *Schall. Ber. Symp. Dtsch. Ges. Metallkd.* 18th, 13/1-4 *(1974).*

[18] V. Mishakin; "Research on the connection between the acoustic parameters of polycrystalline alloys, their plastic characteristics and structural damage." *Acou. Let.,****19(10),*** *192-96 (1996).*

[19] Y. Lin, B. Yan, F. Huang; "Surface modification of Al-Zn-Mg aluminum alloy using the combined process of EDM with USM." *J. Mater. Proc. Tech.,* ***115(3)****, 359-66 (2001).*

[20] S. Zhang, Y. Zhao, X. Cheng, G. Chen, Q. Dai; "High-energy ultrasonic field effects on the microstructure and mechanical behaviors of A356 alloy." *J. Alloys and Comp.,* ***470(1-2),*** *168-72 (2009).*

[21] S. Kolpatzik, A. Schmucker; "Numerical simulation of acoustic signal propagation in ultrasonic flowmeters." *Proc. Int. Gas Res. Conf.,* ***(2),*** *250-60 (1998).*

[22] F. Iacopi, S. Brongersma, A. Mazurenko, G. Antonelli; "Use of SAWs for sub-micron detection of dielectric damage in interconnects for microelectronics." *Proc. IEEE Ultras. Symp.,* ***(1),*** *269-72 (2006).*

[23] L. Jackson; "Solvent cleaning process efficiency." *Adhesives Age.,****19(7)****, 31-4 (1976).*

[24] Q. Wan, A. Kuznetsov; "Numeric modeling of ultrasonic acoustic streaming cooling effect on IC chips." *HTD (Am. Soc. of Mech. Eng.) 369-7 (2001).*

[25] D. Dogas, T. Efthimiopoulos, C. Andreouli, M. Campbell; "Acoustic wave monitoring of the excimer laser ablation of YBCO high-Tc superconductor." *App. Phy. A: Mater. Sci. & Proc.,* ***73(3)****, 287-94 (2001).*

[26] M. Yamanishi, K. Yoshida; "Possible application of surface acoustoelectronic interaction to the investigation of semiconductor surface." *Bull. Osaka Uni. Pref, Series A: Eng. and Nat.Sci.,* ***18(2)****, 365-73 (1969).*

[27] F. Hudert, A. Bartels, K. Koehler; "Influence of doping profiles on coherent acoustic phonon detection and generation in semiconductors." *J. App. Phy.,* ***104(12),*** *123509/1-5 (2008).*

[28] R. Fonseca, J. Saurel, G. Despaux, A. Foucaran, E. Massonne, T. Taliercio, P. Lefebvre; "Elastic characterization of porous silicon by acoustic microscopy." *Superlatt. and Microstru.,* ***16(1)****, 21-3 (1994).*

[29] H. Glyde, M. Klein; "Anharmonic effects and the lattice dynamics of insulators." *CRC Criti. Rev. in Solid State Sci.,* ***2(2),*** *181-254 (1971).*

[30] V. Tartachnik, O. Gontaruk, R. Vernydub, A. Kryvutenko, Y. Olikh, V. Opilat, I. Petrenko, M. Pinkovska; "Radiation-acoustic treatment of gallium phosphide light diodes." *Proc. of SPIE Int. Soc. Opt. Eng.,* ***3890****, 559-63 (1999).*

[31] V. Singh, A. Prasad, Y. Yadav; "Ultrasonic stress effect on a germanium based junction transistor." *Acustica. 71(1), 79-80 (1990).*

[32] S. Niyogi, P. Roy, M. Roychaudhuri; "Acousto-ultrasonic study on hydration of portland cement." *Cera. Trans., 16(Adv. Cem. Mater.), 137-45 (1991).*

[33] J. Ranachowski, F. Rejmund; "Acoustic emission in thermomechanical studies of Ceramics and cement Material." *Prace Komisji Nauk Cera.znych, Cera. (Polska Akademia Nauk), 45(Nowoczesne Materialy i Kompozyty), 177-86 (1994).*

[34] M. Ohtsu, M. Shigeishi, M. Munwam; "Damage mechanics and fracture mechanics of concrete by SiGMA." *J. Acou. Emis.,* ***16(1-4)****, S65-74 (1998).*

[35] J. Craver; "Ultrasonic impedometric studies in the cellulose pulp water system." *Consol. Pap. Web, Trans. Symp.,* ***1****, 445-72 (1966).*

[36] J. Dion, J. Garceau, J. Morissette; "Acousto-optical evaluation of fiber size in wood pulp." *Proc. SPIE Int. Soc. Opt. Eng., 665 (Opt. Tech. Ind. Insp.), 361-65 (1986).*

[37] T. Moran, N. Batra, F. Bucholtz, R. Thomas; "Elastic properties of manganese(II) oxide-alumina-silica glasses." *J. Ultrason. Symp. Proc, 506-8 (1974).*

[38] J. Berret, J. Pelous, R. Vacher, A. Raychaudhuri, M. Schmidt; Acoustic properties and relationship with the low frequency light scattering in an optical glass." *J. Non-Cryst. Solids.* ***87(1-2)****, 70-85 (1986).*

[39] A. Kezionis, A. Orliukas, V. Samulionis, W. Jakubowski, W. Bogusz, B. Wnetrzewski; "Electrical and ultrasonic properties of AgI, AgPO3 glasses." *Lietuvos Fizikos Zurnalas.* ***35(3)****, 202-5 (1995).*

[40] P. Vasantharani, K. Karthikeyani, Vijayakumari; "Thermal expansion and acoustical properties of zinc bismuth borate glasses." *Bull. Pure & App. Sci., Sec. D: Phy.,* ***26D(2)****, 67-72 (2007).*

[41] K. Mehrotra, S. Upadhyaya; "Acoustical studies of calcium soaps." *Acou. Lett.* ***11(4),*** *66-71 (1987).*

[42] K. Mehrotra, R. Shukla, M. Chauhan; "Ultrasonic studies on neodymium soap solutions." *Acustica,* ***75(1),*** *82-5 (1991).*

[43] K. Mehrotra, M. Jain; "Ultrasonic measurements of chromium(III) soaps in chloroform." *Acou. Lett.,* ***18(3),*** *50-4 (1994).*

[44] K. Mehrotra, M. Anis; "Apparent molar volume and acoustic behavior of zirconyl soap solutions in benzene-chloroform mixture." *J. Ind. Chem. Soc.,* ***74(9),*** *720-22 (1997).*

[45] S. Upadhyay, R. Shukla, G. Sharma; "Acoustic behaviour of dysprosium soaps in methanol." *A. J. Chem.,* ***19(4)****, 2993-98 (2007).*

[46] J. Brooks, J. Gormly, W. Sackett; "Molecular and isotopic composition of two seep gases from the Gulf of Mexico." *Geophy. Res. Lett.,* ***1(5),*** *213-16 (1974).*

[47] A. Santos, S. Caetano, M. Andrino, D. Bray, R. Trevisan; "Evaluation of the rolling direction effect in the acoustoelastic properties for API 5L X70 steel used in pipelines." *PVP (Am. Soc. of Mech. Eng.)* ***484,*** *85-90 (2004).*

[48] P. Pena, Ivascan, L. Georgescu, V. Iacob; "Investigations reffering to utilization of the ultrasonic devices to prevent depositions in oil refining plants." *Analele Stiintifice ale Universitatii "Al. I. Cuza" din Iasi, Chimie,* ***13****, 113-20 (2005).*

[49] B. Anderson; "Technical plan for nondestructive examination technology development." *Avail. NTIS. Rep, 33 (1982).*

[50] J. Yan, D. Li, Z. Dong, Y. Zhen; "Analysis and measurement of acoustic power in plastics ultrasonic welding process." *China Welding,* ***7(2),*** *106-11 (1998).*

[51] R. Freemantle, T. Alper, R. Challis; "A model fitting approach to the broad band measurement of ultrasonic wave velocities in thin samples of eng. material." *Meas. Sci. and Tech.,* ***4(10)****, 1129-37 (1993).*

[52] E. Mori, S. Isshiki, T. Shiromizu, S. Yamamoto, S. Mori, K. Iwanabe, H. Oshima, M. Ida, T. Iida; "The new cross-linking method of cross-linked polyethylene cables with ultrasonic wave." *Fujikura Tech. Rev.,* ***(6)****, 40-57 (1974).*

[53] J. Szelazek; "Ultrasonic measurement of thermal stresses in continuously welded rails." *NDT&E Int.,* ***25(2)****, 77-85 (1992).*

[54] R. Koerner, A. Lord, E. Arthur; "Nondestructive testing methods of detecting buried wastes." *Chem. Eng. Prog.,* ***81(3),*** *39-42 (1985).*

[55] A. Tiehm, K. Nickel, U. Neis; "The use of ultrasound to accelerate the anaerobic digestion of sewage sludge." *Water Sci. and Tech.,* ***36****, 121-28 (1997).*

[56] D. Casadonte, M. Flores, C. Petrier; "The use of pulsed ultrasound technology to improve environmental remediation: a comparative study." *Environ. Tech.,* ***26(12)****, 1411-18 (2005).*

[57] G. Cappelletti, S. Ardizzone, C. Bianchi, S. Gialanella, A. Naldoni, C. Pirola, V. Ragaini; "Photodegradation of pollutants in air: enhanced properties of

nano-TiO2 prepared by ultrasound." *Nanoscale Res. Lett., **4(2),** 97-105 (2009).*

[58] A. Isayev, S. Yushanov, S. Kim, V. Levin; "Ultrasonic devulcanization of waste rubbers: experimentation and modeling." *Rheologica Acta (1996), **35(6)**, 616-30.*

[59] V. Yashin, A. Isayev; "A model for rubber degradation under ultrasonic treatment: Part I. Acoustic cavitation in viscoelastic solid." *Rubber Chem. and Tech., **72(4)**, 741-57 (1999).*

[60] K. Seklon, R. Binder; "Ultrasonic techniques to measure water pollutants." *Joint Conf. Sensing Environ. Poll. [Proc.], 2nd, 177-84 (1973).*

[61] L. Turai, R. Del; "Ultrasonic oxidation of chlorinated phenols found in wastewater." *Appita (1982), **35(5)**, 407-11.*

[62] E. Gonze; "Design and characterization of high-frequency ultrasonic reactors for wastewater treatment." *Recent Res. Dev. in Chem. Eng., **4(1)**, 137-60 (2000).*

[63] M. Dehghani, G. Jahed, A. Mesdaghinia, S. Nasseri; "Using irradiation treatment for reduction of anaerobic bacteria from a wastewater treatment plant." *Env. Tech., **29(11)**,1145-48 (2008).*

[64] W. Busch, K. Staffeldt, S. Fertil; "Early diagnosis of molar pregnancy by ultrasonic investigation and HCG [human chorionic gonadotropin] excretion." *Proc. World Congr., 7th, 831 (1973).*

[65] M. Pery, J. Kaftori, J. Bar-Maor; "Sonography for diagnosis and follow-up of neonatal adrenal hemorrhage." *J. clin. Ultra. : JCU, **9(7)**, 397-01 (1981).*

[66] J. Sakamoto, H. Jason, B. Smith, B. Xie, S. Rokhlin, S. Lee, M. Ferrari; "The molecular analysis of breast cancer utilizing targeted nanoparticle based ultrasound contrast agents." *Tech. in Can. Res. & Treat., **4(6)**,627-36 (2005).*

[67] F. Mitri, B. Davis, J. Greenleaf, M. Fatemi; "In vitro comparative study of vibro-acoustography versus pulse-echo ultrasound in imaging permanent prostate brachytherapy seeds." *Ultras., **49(1)**, 31-8 (2009).*

[68] A. Walmsley. A. Williams, W. Laird; "Acoustic absorption within human teeth during ultrasonic descaling." *J. dent., **14(1)**, 2-6 (1986).*

[69] S. Sorenson, D. von Tabouillot, V. Schioler, G. Greisen, S. Petersen, T. Larsen; "Serial measurements of serum human placental lactogen (hPL) and serial ultrasound examinations in the evaluation of fetal growth." *Early Human Develop., **60(1)**, 25-34 (2000).*

[70] S. Stapleton, H. Goodman, Y. Zhou, Q. Yu, E. Cherin, R. Henkelman, P. Burns, F. Foster; "Acoustic and kinetic behaviour of definity in mice exposed to high frequency ultrasound." *Ultras. in med. & bio., **35(2)**, 296-07(2009).*

[71] V. Fasano S. Zeme, L. Frego, R. Gunetti; "Ultrasonic aspiration in the surgical treatment of intracranial tumors." *J.of neurosurgical sci., **25(1)**, 35-40 (1981).*

[72] A. Watanabe, H. Nishimura, N. Kawashima, S. Takeuchi; "Consideration on suppression of cancer cell proliferation by ultrasound exposure using sonochemical and biological measurements." *J. Phy.: Conf. Series, **1**, 210-15 (2004).*

[73] S. Majumdar, d. Willingdon; "The gifts of Phy. to modern medicine." *Everyman's Sci., **40(3)**, 162-78 (2005).*

[74] P. Golla, H. Johnson, P. Senthilnathan; "Application of electro acoustics for dewatering pharmaceutical sludge." *Environ. Prog., **11(1),** 74-9 (1992).*

[75] V. Krasovskii; "Infrasonic variations of hydroxyl emission in the upper atmosphere." *Ann. de Geophy., **28(4),** 739-46 (1972).*

[76] A. Khair; "Correlations of AE signatures to mechanical and petrologic properties of four types of rocks." *J. Acou. Emi. **16(1-4)**, S53-S64 (1998).*

[77] B. Woodward, R. Chandra; "Underwater acoustic measurements on polyvinylidene fluoride transducers." *Ele.Sci. and Tech., **5(3)**, 149-57 (1978).*

[78] P. Brewer, B. Chen, R. Warzinski, A. Baggeroer, E. Peltzer, R. Dunk, P. Walz; "Three-dimensional acoustic monitoring and modeling of a deep-sea CO2 droplet cloud." *Geophy. Res. Let., **33(23)**,L23607/1-5 (2006).*

[79] H. Mizutani, D. Newbigging; "Elastic wave velocities of Apollo 14, 15, and 16 rocks." *Proc. Lunar Sci. Conf., 4th, **3**, 2601-9 (1973).*

[80] W. Cai, V. Yang; "Transient combustion response of AP/HTPB composite solid propellant to acoustic oscillations in a rocket motor." *JANNAF 37th Comb. Subcommittee Meeting.**(1),** 759-86 (2000).*

[81] R. Hanstock; "Development of radiographic and ultrasonic methods of inspecting nuclear reactor pressure vessels." *Non-Destr. Test. in Nuc. Tech. Proc. Sym. on Non-Dest. Test. in Nuc. Tech., 249-54 (1964).*

[82] W. Carey, A. Gavin, J. Bobis, S. Sheen, T. Anderson, R. Doolittle, R. Albrecht; "The detection of sodium vapor bubble collapse in a liquid metal fast breeder reactor." *Prog. Nuc. Ene., **1(2-4)**, 437-68 (1977).*

[83] B. Raj, D. Bhattacharya, P. Rodriguez; "Development of in-service inspection techniques for nuclear power plants in India." *Int. J. Pres. Vess. and Pip., **56(2),** 183-211 (1993).*

[84] I. Sutokskaya; "Effect of ultrasonics on microbial cells (fungi and bacteria)."*Eur. Biophys. Congr, Proc., 1st, **2**, 431-4 (1971).*

[85] J. Henaff, M. Feldmann; "SAW propagation in BANANA." *Ultra. Symp. Proc., **1,** 394-8 (1982).,*

[86] S. Zakharov, K. Bogdanov, L. Rosenshtraukh, L. Gavrilov, V. Yushin; "The effect of acoustic cavitation on the contraction force and membrane potential

of rat papillary muscle." *Ultra.in med. & bio., **15(6)**, 561-5 (1989).*

[87] M. Barany, F. Finkelman; "Lability of the bound calcium of F-actin under ultrasonic vibration." *Biochem. Mus. Contr., 173-7 (1964).*

[88] *M.* Freese, M. Hamid; "Lipid content determination in whole fish using ultrasonic pulse backscatter." *J. Ultrason. Symp. Proc., 69-76 (1974).*

[89] R. Clegg; "Lipoprotein lipase in 'Christiesomes' from goats' milk: a membrane-bound enzyme." *Biochem. Soc. Trans., **6(6),** 1205-7(1978).*

[90] A. Stravs A. Pittet, U. Stockar, P. Reilly; "Measurement of interfacial areas in aerobic fermentations by ultrasonic pulse transmission." *Biotech. and bioeng., **28(9)**, 1302-9 (1986).*

[91] M. Postema, O. Gilja; "Ultrasound-directed drug delivery." J. *Cur. Pharm. Biotech., **8(6)**, 355-61 (2007).*

[92] E. Blomme, D. Bulcaen, F. Declercq, P. Lust; "Air-coupled ultrasonic evaluation of coated textiles." *Proc. IEEE Ultras. Symp., **(1)**, 757- 60 (2002).*

[93] S. Perincek, A. Uzgur, K. Duran, A. Dogan, A. Korlu, I. Bahtiyari, A. Emel; "Design parameter investigation of industrial size ultrasound textile treatment bath." *Ultras. Sonochem, **16(1)**, 184-9 (2009).*

[94] P. Hoare; "Milk and dairy products." *Reports on the Prog. of App. Chem., **51**, 359-66 (1966).*

[95] E. Kress; "Ultrasound propagation in foods and ambient gases: Principles and applications." *Instru. and Sensors for the Food Ind., (2nd Ed.) 355-402 (2001).*

[96] F. Espinosa, A. Montero, L. Elvira, B. Faiz, P. Resa, A. Moudden; "Simultaneous observation of milk coagulation by echography, ultrasonic propagation and thermography." *Proc.IEEE Ultras. Symp, **(1)**, 885-88 (2002).*

[97] G. Savaroglu, E. Aral; "Acoustic parameters of cow's milk added hydrogen peroxide and sodium bicarbonate at different temperatures." *J. Food Eng., **79(1)**, 287-92 (2007).*

[98] J. Riener, F. Noci, D. Cronin, D. Morgan, J. Lyng; "Characterisation of volatile compounds generated in milk by high intensity ultrasound." *Int. Dairy J., **19(4)**, 269-72 (2009).*

[99] B. Tiwari, K. Muthukumarappan, C. O'Donnell, P. Cullen; "Inactivation kinetics of pectin methylesterase and cloud retention in sonicated orange juice." *Inno. Food Sci. & Emer. Tech., **10(2)**, 166-71 (2009).*

[100] E. Henneke, A. Vary, A. Tiwari; "Modeling of stress-strain response of Ceramic composites by acousto-ultrasonic parameters." *NASA Conf. Pub., 19117 (Hightemp. Rev. 1993, 1), 25/1-8 (1993).*

[101] R. Rodriguez, E. Arteaga, D. Rangel, R. Salazar, S. Vargas, M. Estevez; "Mechanical, chemical and acoustic properties of new hybrid Ceramic-

polymer varnishes for musical instruments." *J. Non-Cryst. Solids,* ***355(2)****,132-40 (2009).*

[102] A. Das, S. Niyogi, S. Mukherjee; "Acousto-ultrasonic study of thermal shock damage in castable refractory." *J. Mater. Sci. Letters,* ***10(3)****, 173-5 (1991).*

[103] D. Bell, A. Deighton, F. Palin; "Non-destructive testing of refractories." *Adv. in Refra. for Metall. Ind. II, Proc. of the Int. Symp. on Adv. in Refra. for Metallurgical Industries, 2nd, 191-207(1996).*

[104] G. Mansfeld, S. Alekseev, Y. Gulyaev, Z. Kosakovskaya; "Microwave HBAR spectroscopy and transducer application of carbon nanotube films." *Proc.IEEE Ultras. Sym.,* ***(1)****, 561-64 (1999).*

[105] E. Sekreta, H. Ichitsubo, Y. Kuriki, K. Shimada, K. Uchida, A. Kawai, S. Oshima, M. Yumura; "The synthesis of MoS2 nanoparticles using ultrasonic cavitation." *Trans. of the Mater. Res. Soc. Japan,* ***27(1)****, 93-6 (2002).*

[106] R. Singh, R. P. Singh, M. P. Singh; "Acoustical characterization of nanostructured metal." *Int. J. Nanosci.,* ***7(6)****, 315-23 (2008).*

[107] S. Schramek, E. Visacka, R. Brezina; "Isolation of peptidoglycan from Coxiella burnetii." *Proc. Int. Symp., 2nd 129-33 (1978).*

[108] P. Stumpf D. Green, F. Smith; "Ultrasonic Disintegration as Method of Extracting Bacterial Enzymes." *J. bacteriology* ***51(4)****, 487-93 (1946).*

[109] S. Nii, K. Matsuura, T. Fukazu, M. Toki, F. Kawaizumi; "A novel method to separate organic compounds through ultrasonic atomization." *Chemi. Eng. Res. and Des.,* ***84(A5)****, 412-15 (2006).*

[110] T. Matsunaga, K. Ogata, T. Hatayama, K. Shinozaki, M. Yoshida; "Effect of acoustic cavitation on ease of infiltration of molten aluminum alloys into carbon fiber bundles using ultrasonic infiltration method." *Compo. A: App. Sci. and Manu.,* ***38A(3)****, 771-78 (2006).*

[111] K. Pant, S. Mushran; "Effect of ultrasonic waves on the catalytic activity of hydrous zirconium oxide." *J.Ind. Chem. Soc.,* ***43(12)****, 737-41(1966).*

[112] H. Takeuchi, K. Yamashita;"Surface acoustic wave characteristics of cuprous chloride." *J. App. Phy.,* ***52(12)****, 7448-9 (1981).*

[113] K. Mehrotra, M. Rawat; "Ultrasonic and viscometric studies of manganese dicaprate in organic solvents." *Ind. J. Pure and App. Phy.,* ***29(2)****, 131-3 (1991).*

[114] G. Benedetto, R. Gavioso, R. Spagnolo, P. Marcarino, A. Merlone; "Acoustic measurements of the thermodynamic temperature between the triple point of mercury and 380 K." *Metrologia,* ***41(1)****, 74-98 (2004).*

[115] R. Linde, A. Sliwinski; "The velocity of propagation and attenuation of ultrasound in methylpyridines." *Archives of Acou.,* ***3(1)****, 67-70 (1978)*

[116] P. Agrawal, M. Narwade; "Prediction of viscosity and ultrasonic behavior of substituted flavone, isoxazole and pyrazole in 70% acetone water mixture."

*Acta Cien. Ind., Chem., **28(3)**, 163-66 (2002).*

[117] S. Ravichandran, K. Ramanathan; "Ultrasonic study and allied properties of cholesterol in chloroform solutions at 294K." *J. Pure and App. Ultra., **28(2-4)**, 40-5 (2006).*

[118] R. Baskaran, T. Kubendran, "Refractive indices, ultrasonic velocities, surface tension and thermo acoustical parameters of anisaldehyde + benzene at 323.15K." *Mod. App. Sci., **2(5)**, 91-5 (2008).*

[119] M. Aminuzzaman, M. Khan, M. Uddin; "Effect of ultrasonics on the ciscosity of long-chain polymer solutions. I. 250 Parts poly(oxyethylene) per million parts of water." *Pak. J. Sci. and Ind. Res., **15(6)**, 393-6 (1972).*

[120] I. Alig, D. Lellinger, "Ultrasonic spectroscopy for measurement of phase velocity and attenuation at high frequencies in polymer systems." *Acus., **76(6)**, 273-82 (1992).*

[121] J.Luo, Y. Liu, Y. Fu, J. Xie; "Research development of effect of ultrasonic on polymer extrusion moulding." *Jueyuan Cailiao, **41(5)**, 56-59 (2008).*

[122] M. Labowski; "Acoustic study of critical nitrobenzene-n-heptane mixture throughout a wide range of frequencies." *Acou. Lett. **3(2)**, 37-42 (1979).*

[123] B. Koul, R. Wanchoo, T. Razdan, R. Murti, P. Khosa; "Ultrasonic study of a binary liquid mixture: benzene-ethylacetate." *Acustica, **58(2)**, 101-4(1985).*

[124] S. Mirzaev, P. Kikhabibullaev, A. Asaidov; "Critical properties of acoustic wave absorption: in the critical methanol-cyclohexane mixture." *Uzbek. Fiziche. Zhur., **(5)**,31-7 (1998).*

[125] V. Syal, A. Chauhan, P. Sharma, S. Chauhan; "Ultrasonic velocity and viscosity studies on solutions of poly(vinylalcohol) (PVA) in binary mixtures of DMSO + H2O at 25°C." *J. Poly. Mat., **22(4)**, 363-68 (2005).*

[126] S. Azhagiri, S. Jayakumar, R. Padmanaban, S. Gunasekaran; "Acoustic and Thermodynamic Properties of Binary Liquid Mixtures of Benzaldehyde in Hexane and Cyclohexane." *J. Sol. Chem., **38(4)**,441-48 (2009).*

[127] S. Bhatti and K. Prabhakar; "Acoustical and optical investigations of a ternary liquid mixture at its miscibility point." *Ind. J. Phy., **69B(5)**, 389-98 (1995).*

[128] J. Daridon, B. Lagourette, A. Lagrabette; "Acoustic determination of thermodynamic properties of ternary liquid mixtures up to 150 MPa." *Phy. and Chem. Liq., **37(2)**, 137-60 (1999).*

[129] K. Ali, K. Tiwari, A. Nain, V. Chakravortty; "Ultrasonic study of molecular interactions in ternary mixtures of dimethyl sulphoxide (1) + carbon tetrachloride (2) + aromatic hydrocarbons at 308.15." *Ind. J. Phy., **74B(5)**, 351-55 (2000).*

[130] K. Vijayalakshmi, V. Lalitha, R. Gandhimathi; "Acoustic and excess parameter studies on interaction in ternary liquid mixtures." *J. Pure and App. Ultra., **28(2-4)**, 154-56 (2006).*

[131] S. Baluja, F. Karia; "Theoretical evaluation of ultrasonic velocities in quaternary systems." *Asian J. Chem., **12(4)**, 1167-72 (2000).*

[132] S. Baluja and A. Shah; "Acoustical studies of schiff bases in 1,4-dioxane and dimethylformamide at 318.15 K" Russi. J. Phy. Chem. **80**, 7, 1056-60(2006)

[133] S. Baluja, N. Vekariya and J. Movaliya; "Acoustical studies of some derivatives of 4-amino benzoic acid in 1, 4-dioxane and dimethyl formamide at 308.15 k" Iran. J. Chem. and Chem. Eng., **27**, (1)129-35 (2008).

[134] S. Baluja, N. Kachhadia and A. Solanki; "Thermodynamic studies of some 1,2,4-triazole derivatives in DMF and THF solutions at 308.15 K." *Phy. and Chem. Liq.,* **45**, *(5) 561-69 (2007)*

[135] S. Baluja and S. Oza; "Ultrasonic studies of some derivatives of sulphonamide in dimethylformamide" *Fluid phase equi*., **200,** 11-18 **(**2002)

[136] S. Baluja, J. Movaliya and N. Godvani; "Acoustical studies of some derivatives of 1,5-benzodiazipines at 298.15 K." *Proceedings of the 3rd Naional Conference on Thermo. of Chem. Bio. Systems.NCTCBS-2008* 133-38 (2008)

[137] J. A. Riddick, W. B. Bunger, T. Sakano, Organic Solvents: Physical Properties and methods of purification, Fourth Edition., Techniques of Chemistry, **II**, A Wiley-Interscience Publication, John Wiley, New York (1986).

[138] L.Ubbelhode; "Theory of the Friction of Lubricated Machine Parts" *Petroleum*., **7,** 882-89 (1912).

[139] R. A. Robinson, R. H. Stokes; "Electrolyte Solutions." *Butterworths Scientific Publications, London* (1955).

[140] G. L. Sastry, V. K. Sastry, B. Krishnamurty; "Ultrasonic parameters in mixed salt solutions." *Ind. J. Pure Appl. Phy*., **6**, 637-38 (1968).

[141] B. Jacobson; Nature (London), **173,** 772 (1954).

[142] Y. Wada; "The relation between compressibility and molal volume of organic liquids" *J. Phy. Soci. Jap*., **4**, 280-83 (1949).

[143] S. Sendhilnathan, S. Bagchi, S. K. Nema, R. P. Singh; "Ultrasonic and rheological investigations of solid propellant binders" *Euro. Poly. J*., **25**, 441-44 (1989).

[144] P. Vigoureux; "Ultrasonics", Chapman and Hall, London (1952).

[145] G. K. Johri, R. C. Misra; *Acustica*, **57**, 292 (1985).

[146] C. Bachem; "Z. Electrochem." **41**, 570 (1935).

[147] F. T. Gucker (Jr.), "The apparent molal heat capacity, volume and compressibility of electrolytes" *Chem. Rev*., **64**, 111-30 (1993).

[148] D. Jones and M. Dole; "Viscosity of aqueous solutions of strong electrolytes with special reference to barium chloride." J. Am. Chem. Soc., **51**, 2950-64(1929).

INTRODUCTION

The refractive index is the characteristics of a given material. It can be defined as ratio of speed of light in vacuum to its speed in given material. The refractive index of a material is the most important property of any optical system that uses refraction.

A refractometer is the instrument used to measure refractive index. Different methods have been developed to measure the refractive index of liquids. The most common type of refractometer measures the refractive index of the samples by detecting the critical angle of total reflection.

The applications of refractive index in physics [1-3], biology [4-5], mineralogy [6-7] and chemistry [8-9] play an important role in this era. In medicine, particularly ophthalmology and optometry, the technique of refractometry utilizes the property of refraction for eye drops [10]. It is used to calculate the focusing power of lenses [11-12], the visual appeal and characteristics of a gemstone [13-15] Also, knowledge of the refractive index of various substances is used to evaluate the purity of a substance or measure its concentration in a mixture [16-17]. In the field of biochemistry, refractive index is used in various different solutions of biological agents[19]. Chemical modifications may also be detected by measurements of refractive index [20]. Among the many possible applications is the control of adulteration of liquids. [21]

More over, it is also useful in various Industries of beverages [22-23], chemical [24], cosmetics [25-26], food [27-28], minerals [29], mining [30-31], textiles [32-33], petroleum [34], pharmacy [35-36] etc. Also used for environmental study [37-40] purpose to measure various pollutants.

Further, molar refraction has been useful in structural studies. The molar refraction increases in regular increments with the number of carbon atoms within a homologous series. So, molar refraction of the compound can be considered as the sum of atomic increments and that, within certain limits, the contribution of each atom is the same in every molecule [18].

Many workers have reported refractive index of oils [41-42], amino acid [43], protein [44], sugar [45-46], liquid crystals [47], various gases [48], other

materials [49-51] etc. Further, much work has been done in liquid mixtures [52-55] but scanty work has been reported for the solutions of organic [56-58], inorganic [59-62], polymeric materials [63-64] and ionic liquid [65]

Thus, in the present section, the refractive index of solutions of cyanopyridines has been measured in dimethylformamide and dimethyl sulphoxide at 298.15 K. From the experimental data, the density and refractive index of the compounds have been evaluated.

EXPERIMENTAL

The solvents DMF and DMSO were purified by fractionally distillation by the reported method [66]. For each compound, a series of solutions of different concentrations were prepared in these solvents.

The density and refractive index of pure solvents and solutions were measured by using pycnometer and Abbe refrectometer respectively at 298.15 K. The temperature was maintained by circulating water through jacket around the prisms of refractometer from an electronically controlled water bath (NOVA NV-8550 E). The uncertainty of temperature was ± 0.1 ^{o}C and that of density and refractive index was ±0.0001 g/cm^{3} and 0.0005 respectively.

RESULTS AND DISCUSSION

The density of solution (ρ_{12}) is related to densities of the solvent, solute and their weight fractions g_1 and g_2 according to the equation:

$$\frac{1}{\rho_{12}} = \frac{g_1}{\rho_1} + \frac{g_2}{\rho_2} \qquad \ldots (3.2.1)$$

where ρ_{12} is the density of solution and ρ_1 and ρ_2 are the densities of solvent and solute respectively. Tables 3.2.1 and 3.2.2 show the experimental values of densities and refractive index for all the studied solutions.

The density of these compounds was determined from the slope of the plot of $1/g_1\rho_{12}$ verses g_2/g_1. Figure 3.2.1 shows the plot of $1/g_1\rho_{12}$ verses g_2/g_1 for CP-1 in DMF and DMSO respectively. The inverse of slope gives the value of ρ_2. The densities of all the compounds (ρ_2) evaluated from such plots are given in Table 3.2.3 in DMF and DMSO solutions. Further, the density of compounds were evaluated by using the following equation (3.2.2),

$$\rho = KM/N_A \sum \Delta V_i \qquad \ldots (3.2.2)$$

where ρ is the density of the compound, K is packing fraction (0.599), M is the molecular weight of the compound, N_A is the Avogadro's number and ΔV_i is the volume increment of the atoms and atomic groups present in the compound. The densities of all the studied compounds have been evaluated and are reported in Table 3.2.3. The calculated volume increment ΔV_i for different atomic groups are given in Table 3.2.4.

Comparison of densities evaluated from graphs and those calculated from eq. (3.2.2) showed that calculated values are different from those evaluated graphically. Further, for the same compound, density in the two solvents is different. This suggests that solvent plays an important role. In solutions, molecular interactions exist which differ in different solvents. These interactions differ due to the presence of different substitutions in compounds. The presence of these interactions has also observed in ultrasonic studies which are discussed in section I of chapter 2. Due to these interactions, there may be some changes in volume which affects density.

Table 3.2.1: The density (ρ_{12}) and refractive index (n) of cyanopyridines in DMF at 298.15K.

Conc. M	ρ_{12} g.cm^{-3}	n	ρ_{12} g.cm^{-3}	n
	CP-1		CP-6	
0.00	0.9439	1.4255	0.9439	1.4255
0.01	0.9447	1.4296	0.9451	1.4265
0.02	0.9455	1.4306	0.9468	1.4273
0.04	0.9463	1.4322	0.9491	1.4288
0.06	0.9474	1.4334	0.9518	1.4297
0.08	0.9529	1.4341	0.9552	1.4309
0.10	0.9587	1.4360	0.9585	1.4324
	CP-2		CP-7	
0.01	0.9455	1.4306	0.9461	1.4264
0.02	0.9467	1.4313	0.9489	1.4268
0.04	0.9483	1.4319	0.9522	1.4271
0.06	0.9507	1.4325	0.9559	1.4286
0.08	0.9549	1.4331	0.9601	1.4303
0.10	0.9598	1.4341	0.9652	1.4322
	CP-3		CP-8	
0.01	0.9488	1.4304	0.9448	1.4268
0.02	0.9528	1.4318	0.9458	1.4278
0.04	0.9593	1.4332	0.9471	1.4289
0.06	0.9615	1.4344	0.9489	1.4301
0.08	0.9629	1.4354	0.9614	1.4314
0.10	0.9691	1.4361	0.9646	1.4329
	CP -4		CP-9	
0.01	0.9471	1.4309	0.9458	1.4263
0.02	0.9482	1.4321	0.9474	1.4270
0.04	0.9497	1.4339	0.9499	1.4282
0.06	0.9513	1.4348	0.9524	1.4293
0.08	0.9532	1.4351	0.9561	1.4306
0.10	0.9551	1.4365	0.9596	1.4321
	CP -5		CP-10	
0.01	0.9445	1.4265	0.9451	1.4268
0.02	0.9454	1.4276	0.9468	1.4274
0.04	0.9467	1.4281	0.9491	1.4280
0.06	0.9480	1.4291	0.9516	1.4287
0.08	0.9542	1.4310	0.9567	1.4291

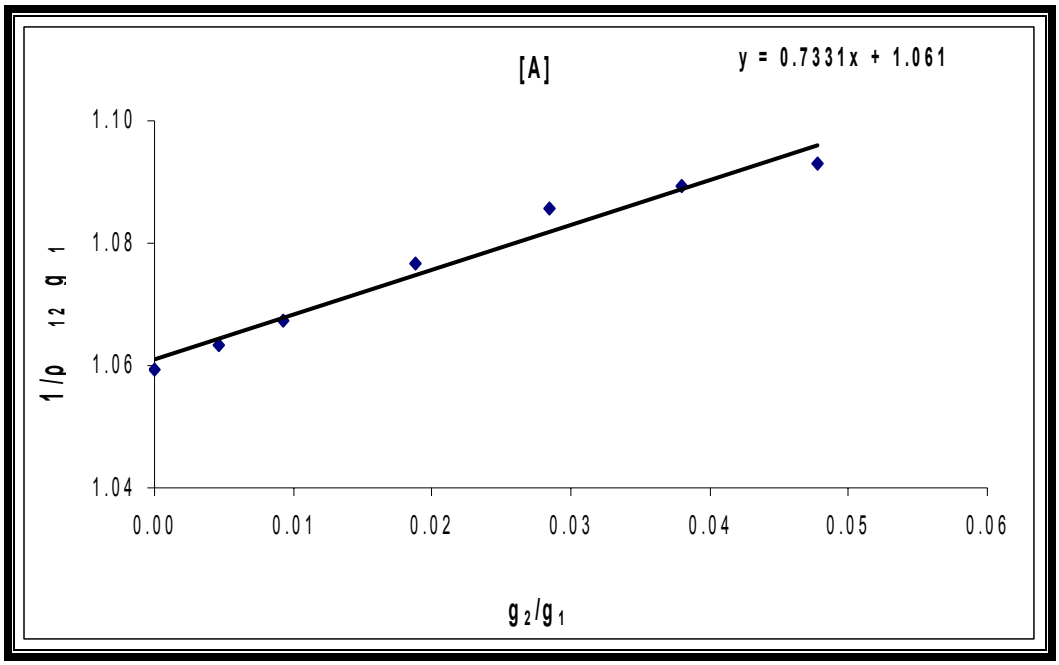
0.10	0.9609	1.4331	0.9612	1.4308

Table 3.2.2: The density (ρ_{12}) and refractive index (*n*) of cyanopyridines in DMSO at 298.15K.

Conc. M	ρ_{12} *g.cm^{-3}*	*n*	ρ_{12} *g.cm^{-3}*	*n*
	CP-1		***CP-6***	
0.00	1.0959	1.4753	1.0959	1.4753
0.01	1.0965	1.4777	1.0963	1.4770
0.02	1.0967	1.4786	1.0965	1.4773
0.04	1.0975	1.4798	1.0969	1.4779
0.06	1.0982	1.4813	1.0974	1.4787
0.08	1.1003	1.4826	1.0980	1.4816
0.10	1.1033	1.4857	1.0988	1.4824
	CP-2		***CP-7***	
0.01	1.0961	1.4779	1.0967	1.4766
0.02	1.0964	1.4784	1.0971	1.4769
0.04	1.0970	1.4803	1.0979	1.4778
0.06	1.0979	1.4829	1.0998	1.4791
0.08	1.0993	1.4841	1.1021	1.4814
0.10	1.1021	1.4868	1.1062	1.4833
	CP-3		***CP-8***	
0.01	1.0975	1.4784	1.0965	1.4764
0.02	1.0989	1.4788	1.0970	1.4770
0.04	1.1002	1.4795	1.0976	1.4777
0.06	1.1028	1.4814	1.0995	1.4790
0.08	1.1069	1.4831	1.1019	1.4799
0.10	1.1132	1.4855	1.1056	1.4831
	CP -4		***CP-9***	
0.01	1.0960	1.4780	1.0964	1.4771
0.02	1.0962	1.4785	1.0967	1.4775
0.04	1.0967	1.4798	1.0972	1.4784
0.06	1.0975	1.4823	1.0979	1.4798
0.08	1.0989	1.4843	1.0986	1.4815
0.10	1.1018	1.4864	1.0999	1.4827
	CP -5		***CP-10***	
0.01	1.0965	1.4765	1.0966	1.4759
0.02	1.0972	1.4769	1.0969	1.4766
0.04	1.0979	1.4778	1.0975	1.4773
0.06	1.0990	1.4792	1.0982	1.4788
0.08	1.1008	1.4809	1.0991	1.4806

0.10	1.1043	1.4833	1.1009	1.4838

Figure 3.2.1: The variation of $1/g_1\rho_{12}$ with g_2/g_1 for CP-1 in [A] DMF and [B] DMSO at 298.15 K.



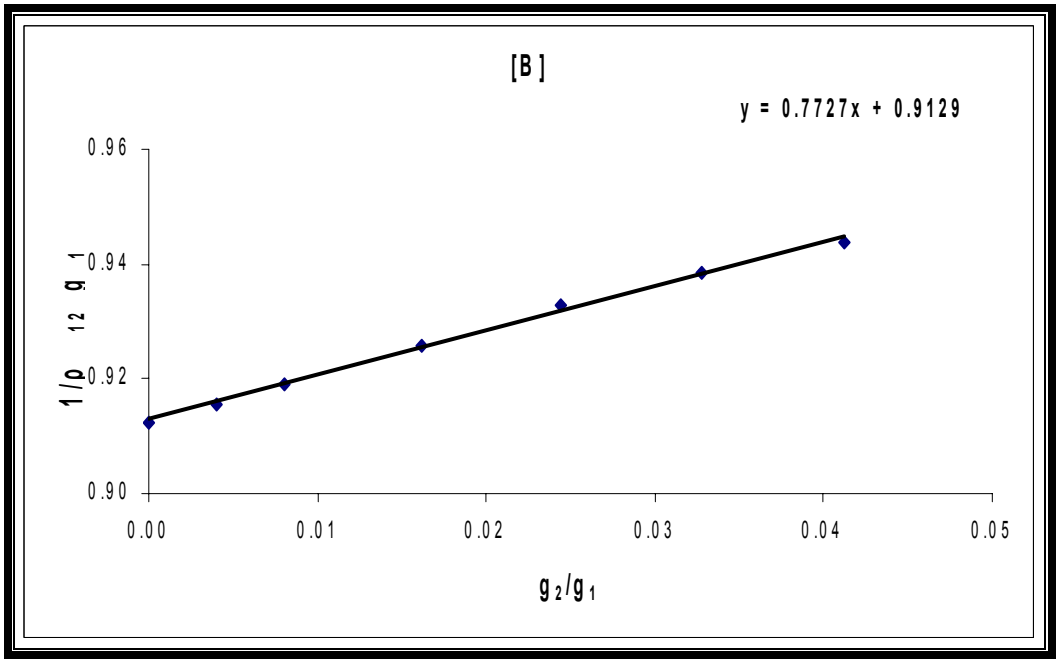
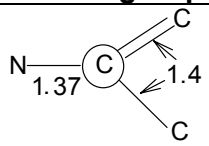
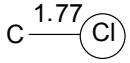
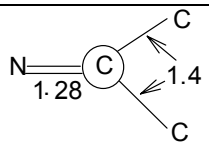
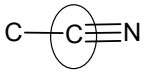
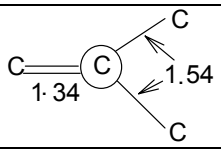
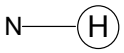
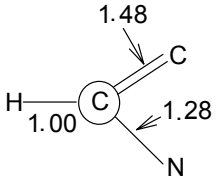
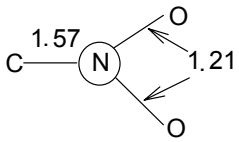
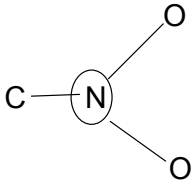
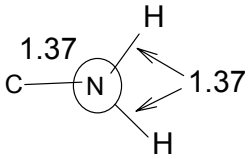
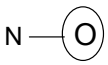
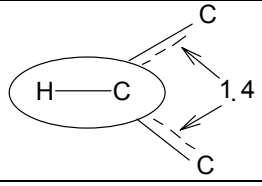
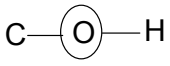
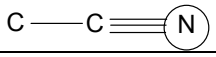
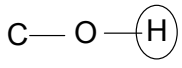
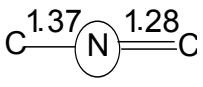
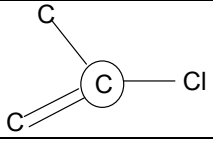
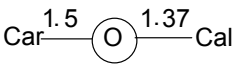
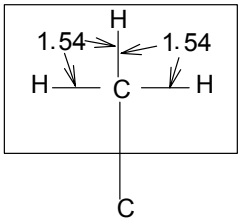
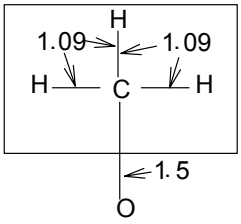
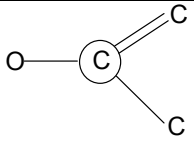


Table 3.2.3: Experimental and calculated densities of cyanopyridines in DMF and DMSO Solutions at 298.15 K.

Compounds	Density ($g.cm^{-3}$) calculated from Figure 3.2.1		Density ($g.cm^{-3}$) Calculated from Eq^{n}. 3.2.2
	DMF	*DMSO*	
CP-1	1.3641	1.2347	1.1673
CP-2	1.4624	1.3201	1.1517
CP-3	1.7806	1.3168	1.2990
CP-4	1.2361	1.3006	1.1928
CP-5	1.5218	1.3355	1.2354
CP-6	1.4378	1.3029	1.9530
CP-7	1.8005	1.2999	1.2162
CP-8	1.7737	1.3186	1.2350
CP-9	1.4689	1.2204	1.1884
CP-10	1.3939	1.1790	1.1665

Table 3.2.4: Volume increments of some atoms and groups of atoms.

Atoms or Atomic group	Volume Increments $(A^o)^3$	Atoms or Atomic group	Volume Increments $(A^o)^3$
	10.2		19.35
	7.84		15.9
	9.0		3.19
	3.61		7.46
	7.46		3.65
	7.29		14.7
	5.6		10.0
	4.7		5.62
	10.39		2.67

Atoms or Atomic group	Volume Increments $(A^o)^3$	Atoms or Atomic group	Volume Increments $(A^o)^3$
	23.5		26.3
	11.65		

Further, the molar refraction of a pure liquid $(MRD)_1$ were calculated by the following equation:

$$\left(MRD\right)_1 = \left[\frac{n^2-1}{n^2+1}\right]\frac{M}{\rho} \qquad \ldots (3.2.3)$$

where n, M and ρ are refractive index, molecular weight and density of pure liquid respectively.

For solutions, following equation was used to determine molar refraction.

$$\left(MRD\right)_{12} = \left[\frac{n_{12}^2-1}{n_{12}^2+1}\right]\left[\frac{X_1M_1+X_2M_2}{\rho_{12}}\right] \qquad \ldots (3.2.4)$$

where n_{12} and ρ_{12} are refractive index and density of solution respectively. X_1 and X_2 are the mole fractions and M_1 and M_2 are the molecular weight of the solvent and solute respectively.

Figures 3.2.2 and 3.2.3 shows the plots of $(MRD)_{12}$ verses concentration for cyanopyridines series in DMF and DMSO respectively. It is evident that $(MRD)_{12}$ increase with the increase in concentration. The molar refraction of solid compounds were determined by following equation:

$$\left(MRD\right)_{12} = X_1\left(MRD\right)_1 + X_2\left(MRD\right)_2 \qquad \ldots (3.2.5)$$

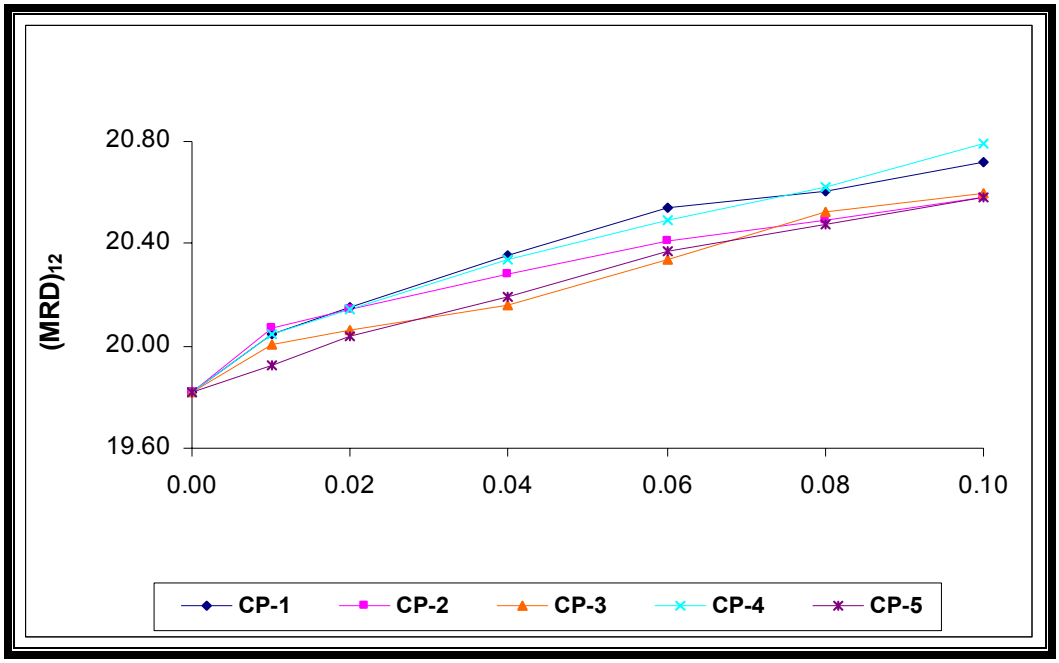
From the density and molar refraction data, the refractive indexes of all the compounds were calculated from eq. (3.2.3). The molar refraction $(MRD)_2$ and refractive index of all the compounds are reported in Table 3.2.5 for 0.1 M solution.

It is evident from Table 3.2.5 that both $(MRD)_2$ and refractive index of compounds are different in each solvent. This again confirms different inter molecular interactions in different solvents. In some solvents, aggregation or hydrogen bonding takes place whereas in others, breakage of bonds may take place.

The studied compounds have different substitutions with the same central moiety. Thus, $(MRD)_2$ and refractive index are affected by

substitutions. It is observed from Table 3.2.5 that molar refraction is affected to a larger extent than the refractive index, which changes only slightly.

Figure 3.2.2: The plots of molar refraction *(MRD)*$_{12}$ against concentration of cyanopyridines in DMF solutions at 298.15 K.



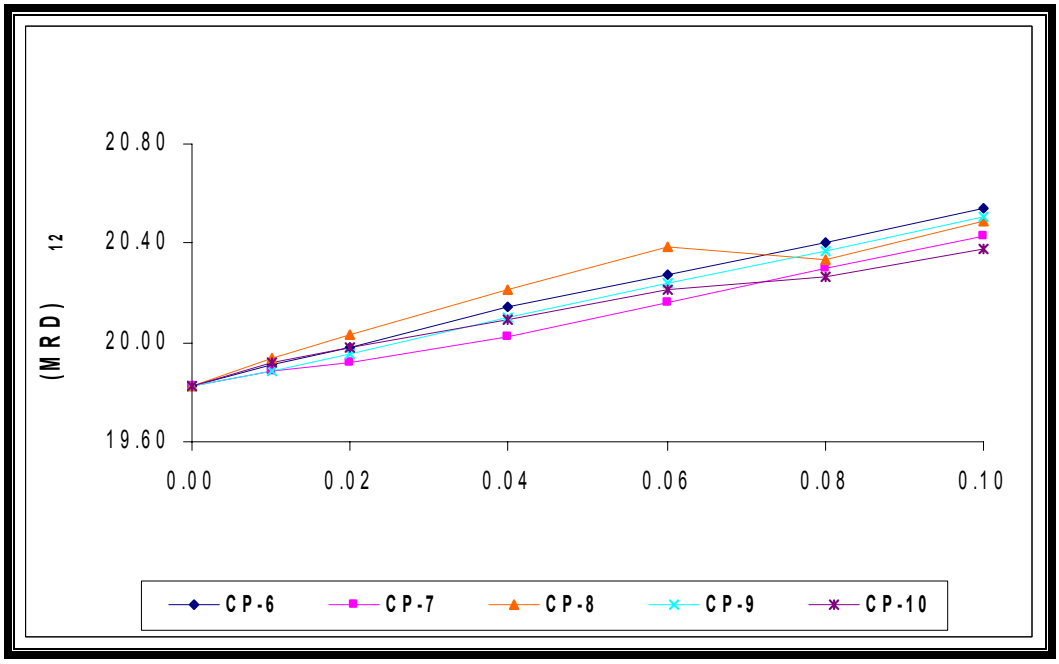
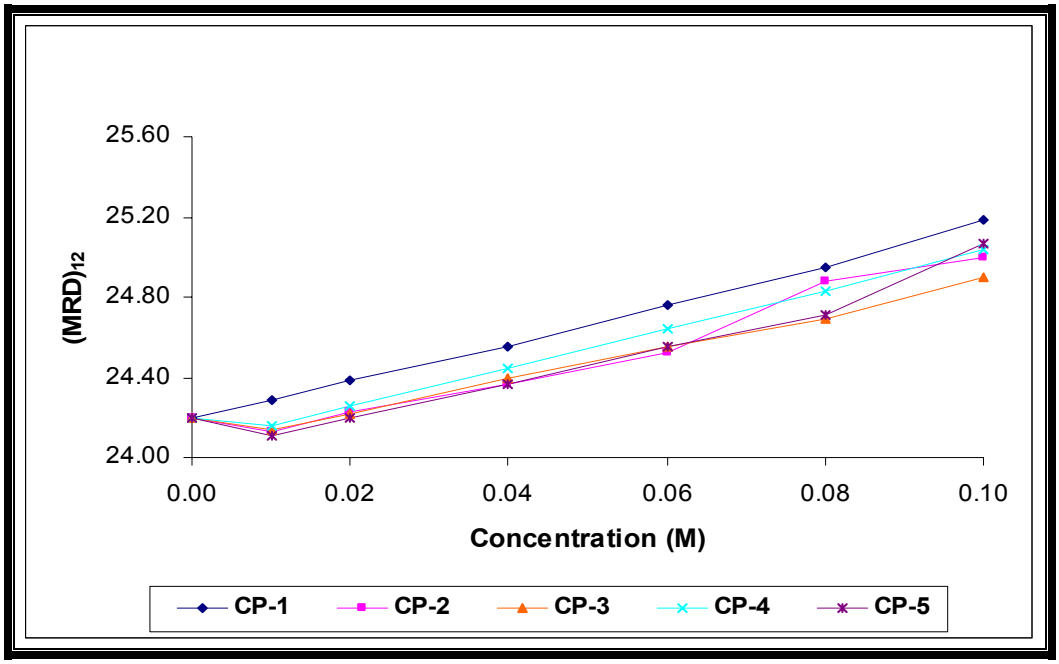


Figure 3.2.3: The plots of molar refraction *(MRD)*$_{12}$ against concentration of cyanopyridines in DMSO solutions at 298.15 K.



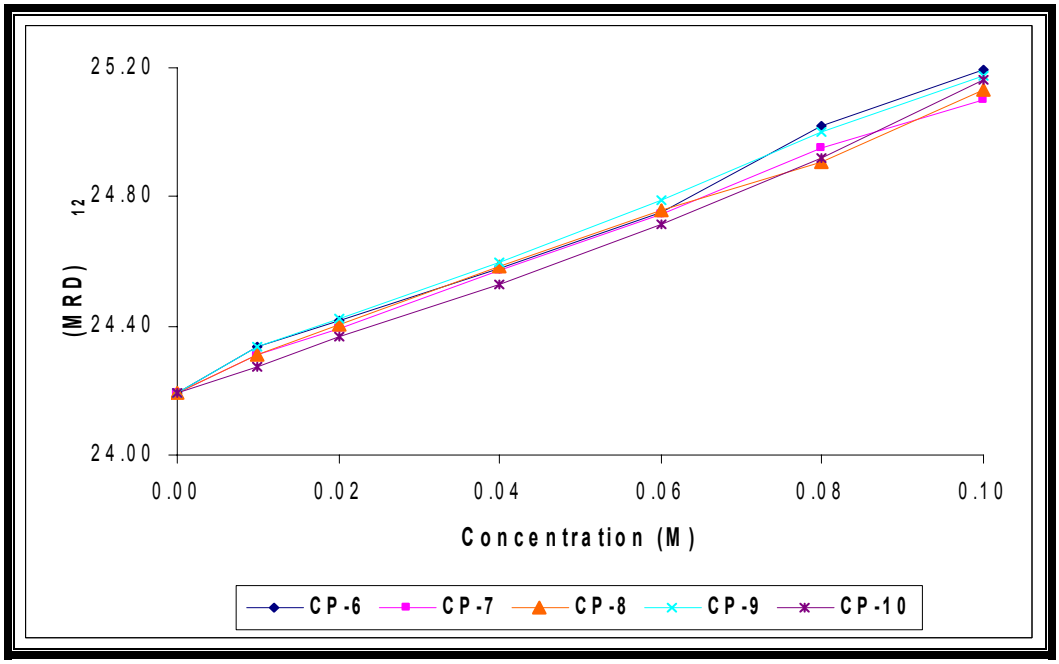


Table 3.2.5: Molar refraction *(MRD)$_2$* and refractive index *(n)* of 0.1M solution of cyanopyridines in DMF and DMSO at 298.15 K.

Compounds	Solvents			
	DMF		DMSO	
	(MRD$_2$)	*n*	*(MRD$_2$)*	*n*
CP-1	133.4178	1.4360	145.9156	1.4857
CP-2	115.8843	1.4341	150.1761	1.4868
CP-3	118.9980	1.4361	132.0298	1.4855
CP-4	142.0063	1.4365	149.7041	1.4864
CP-5	116.0691	1.4331	134.8324	1.4833
CP-6	111.3235	1.4324	137.2403	1.4824
CP-7	97.2410	1.4322	127.6303	1.4833
CP-8	104.9780	1.4329	130.4775	1.4831
CP-9	106.4942	1.4321	135.6687	1.4827
CP-10	90.9953	1.4308	134.5380	1.4838

REFERENCES

[1] T. Töpfer, J. Hein, J. Philipps, D. Ehrt and R. Sauerbrey; "Tailoring the nonlinear refractive index of fluoride-phosphate glasses for laser applications." *App. Phy. B: Lasers & Optics*, ***71 (2),*** *204-9 (2000)*

[2] C. Bertarelli, M. C. Gallazzi, G. Zerbi, E. Molinari, A. Bianco and E. Giro; "Diarylethenes in astrophysics: From materials to devices." *Mol. Cry. Liq. Cry.,* ***430****, 187- 92 (2005).*

[3] R. L. Hammer, W. F. Sherwood, M. S. Faraway and D. E. Nikles; "Polymer waveguides for explosives detection." Abs. 235th ACS Nat. Meeting, New Orleans, LA, U. S., Apr. 6-10, (2008).

[4] J. J. Wang, L. Chen, S. Kwan, F. Liu and X. Deng; "Resonant grating filters as refractive index sensors for chemical and biological detections." *J. Vac. Sci. Tech., B: Microele. Nano. Str.,* ***23(6),*** *3006-10 (2005).*

[5] A. R. Mohammed, S. Eldin, and E. Babiker; "Protein structure, physicochemical properties and mineral composition of Apis mellifera honey samples of different floral origin." Aus. J. Basic App. Sci., ***3(3),*** *2477-83 (2009).*

[6] S. Jochen, P. Dieter and G. Schindler; "Santarosaite, CuB2O4, a new mineral with disordered structure from the Santa Rosa mine, Atacama desert, Chile." *Neues Jahrbuch Min. Abhand.,* ***185(1),*** *27-32 (2008).*

[7] J. Marian, B. Ignac, L. Dusan, S. Vojtech, V. Dusan and C. Dusan; "Terahertz time-domain spectroscopy of selected layered silicates." *Clays and Clay Min.,* ***57(4),*** *416-24 (2009).*

[8] I. G Thapar, V. V Subrahmanyam; "Preparation and physical properties of fatty acid esters of 1,2 propane diol. 1-Monoesters and monoacid diesters." *J. Oil Tech. Ass. Ind.,* ***5(3),*** *36-40 (1973).*

[9] L. Gabriela, C. Silvia and L. Catalin; "Prediction of excess thermodynamic properties from experimental refractive index of binary mixtures." *Rev. Rou. Chimie.* ***53(9),*** *859-67 (2008).*

[10] M. A. Babizhayev; "Ophthalmic pharmacology of N-acetylcarnosine lubricant eye drops." *J. Pharma. Toxi.* ***1(3),*** *201-33 (2006).*

[11] A.R. Cornejo, J.C. Pedraza, A. D. Cordero, F. Cobos; "Measurement of the refractive-index of a lens for one wavelength (6328 .ANG.)." *App. Opt.,* ***20(17),*** *2975-9 (1981).*

[12] R. P. Shukla, G. M. Perera, M. C. George, P. Venkateswarlu; "Determination of refractive index of a simple negative, positive, or zero power lens using wedged plated interferometer." *App. Opt.,* ***29(31),*** *4541-3 (1990).*

[13] N. M. Balzaretti; "Pressure dependence of the refractive index of diamond, cubic silicon carbide and cubic boron nitride." *Solid State Comm., **99(12),** 943-48 (1996).*

[14] T. Ruf, M. Cardona, C. Pickles, R. Sussmann; "Temperature dependence of the refractive index of diamond up to 925 K." *Phy. Rev. B: Cond. Mat. Mate. Phy., **62(24),** 16578-81 (2000).*

[15] A. Brajkovic, V. Rolandi, P. Vignola, R. Grizzetti; "Blue and pink opals from Acari, Peru. Their optical, structural, and spectroscopic features." *Aus. Gemmo., **23(1),** 3-15 (2007).*

[16] M. C. Gerogiannaki, P. E. Athanasopoulos, N. V. Kyriakidis; "Correlation study for the determination of alcoholic strength by the use of pycnometer and refractometer." *Riv. Vitico. Enolo., **55(4),** 57-62 (2002).*

[17] H. Abid, A. Hussain; "Physicochemical characteristics and fatty acid composition of sea-buckthorn (Hippophae rhamnoides L) oil." *J. Chem. Soc. Pak., **29(3),** 256-59 (2007).*

[18] G. Chatwal and S. Anand; " Instrumental methods of chemical analysis" *Himalaya publishing house, 2nd edition, 365, 1984.*

[19] Zocchi, G; "Mechanical measurement of the unfolding of a protein." Europhys. Let., 35, 633-38 (1996).

[20] Barbara, B., Fatme, M., Susan, E. Y., Dennis, T. C., Xavier, L. and Michael, J. C; "Effect of physico-chemical modification on the immunogenicity of Haemophilus influenzae type b oligosaccharide–CRM197 conjugate vaccines." Vaccine, 19, 3189-3200 (2001).

[21] R. S. Costa, S. Santos, L. Almeida, E. Nascimento, M. Pontes, R. Lima, and S. Simoes; "A novel strategy to verification of adulteration in alcoholic beverages based on Schlieren effect measurements and chemometric techniques." *J. Microchem., **78(1),** 27-33 (2004).*

[22] K. Prasad and N. Nath; "Estimation of sugar content in commercially available beverages using ultrasonic velocity measurement." *Ind. J. Phy. A **74A(4),** 387-89 (2000).*

[23] K. Sharma, S. Sharma, S. Lahiri; "Novel method for identification and quantification of methanol and ethanol in alcoholic beverages by gas chromatography-Fourier transform infrared spectroscopy and horizontal attenuated total reflectance-Fourier transform infrared spectroscopy." *J. AOAC Int., **92(2),** 518-26 (2009).*

[24] W. Gao, X. Liu, R. Gross; "Determination of molar mass and solution properties of cationic hydroxyethyl cellulose derivatives by multi-angle laser light scattering with simultaneous refractive index detection." *Poly. Int., **58(10),** 1115-19 (2009).*

[25] V. Andrisano, R. Gotti, D. Pietra, M. Anna and V. Cavrini; "Comparative evaluation of three chromatographic methods in the quality control of fatty alcohols for pharmaceutical and cosmetic use." *Farmaco* ***49(6),*** *387-91 (1994).*

[26] J. Sun, M. Erickson and J. Parr; "Refractive index matching: principles and cosmetic applications." *Cosmet. Toil.,* ***118(1),*** *65-66, (2003).*

[27] "Determination of reducing and non-reducing carbohydrates in food products by liquid chromatography with post-column catalytic hydrolysis and derivatization. Comparison with refractive index detection." R. Femia, R. Weinberger; *J. Chromat.* ***402*** *127-34 (1987).*

[28] M. Kashmiri, M. S. Nawaz, N. Naz; "Physico-chemical analysis of different honey produced in Pakistan." *J. Nat. Sci. Math.,* ***42(1),*** *73-78 (2002).*

[29] K. Kandler, N. Benker, U. Bundke, E. Cuevas, M. Ebert, P. Knippertz, S. Rodriguez, L. Schuetz and S. Weinbruch; "Chemical composition and complex refractive index of Saharan mineral dust at Izana, Tenerife (Spain) derived by electron microscopy." *Atmos. Env.,* ***41(37),*** *8058-74 (2007).*

[30] S. Guggenheim, H. Frimmel; "Ferrokinoshitalite, a new species of brittle mica from the Broken Hill mine, South Africa: structural and mineralogical characterization." *Can. Miner.,* ***37(6),*** *1445-52 (1999).*

[31] S. Mills, U. Kolitsch, R. Miyawaki, L. Groat; "Joelbruggerite, Pb3Zn3(Sb5+,Te6+)As2O13(OH,O), the Sb5+ analog of dugganite, from the Black Pine mine, Montana." *Am. Miner.,* ***94(7),*** *1012-17 (2009).*

[32] M. Lee, Y. Cho, E. Choe and C. Chung; "On-line monitoring of cellulase treatment by differential refractometer." *Fib. and Poly.,* ***8(4),*** *356-62 (2007).*

[33] P. Greaves, O. Microtex; "Alternative and specialised textile fibre identification tests." Woodhead Pub. Text., 84, 181-202 (2009).

[34] G. Song, D. Zhao, M. Hou, Y. Guo; "Study on intensification of catalytic cracking." *Petro. Sci. Tech.,* ***27(13),*** *1429-38 (2009).*

[35] M. Green, H. Nettey, V. Ofelia, C. Pamanivong, L. Khounsaknalath and G. Miguel; "Use of refractometry and colorimetry as field methods to rapidly assess antimalarial drug quality." J. Pharm. Biomed. Ana., ***43(5),*** 1890 (2007).

[36] X. Cao, B. Hancock, N. Leyva, J. Becker, V. Masterson, "Estimating the refractive index of pharmaceutical solids using predictive methods." *Int. J. Pharm.,* ***368(1-2),*** *16-23 (2009).*

[37] A. Virkkula, I. Koponen, K. Teinila, R. Hillamo, V. Kerminen and M. Kulmala; "Effective real refractive index of dry aerosols in the Antarctic boundary layer." Geophy. Res. Lett., ***33(6),*** L06805/1-L06805/4 (2006).

[38] P. Gwaze, G. Helas, H. Annegarn, J. Huth, S. Piketh; "Physical, chemical and optical properties of aerosol particles collected over Cape Town during winter haze episodes." *S. Afr. J. Sci., **103(1/2),** 35-43 (2007).*

[39] R. Ghazy, N. Hendawy, S. Said, H. Nafie, F. El-Mekawey; "Precise determination of refractive index of most popular environmental pollutant gases (1)." *Egy. J. Phy., **39(1),** 11-24 (2008).*

[40] O. Schmid, D. Chand, E. Karg, P. Guyon, G. Frank, E. Swietlicki and M. Andreae; "Derivation of the Density and Refractive Index of Organic Matter and Elemental Carbon from Closure between Physical and Chemical Aerosol Properties." *Env. Sci. Tech., **43(4),** 1166-72 (2009).*

[41] K. Tanilgan, M. Ozcan and A. Unver; "Physical and chemical characteristics of five Turkish olive (Olea europea L.) varieties and their oils." *Grasas y Aceites, **58(2),** 142-47 (2007).*

[42] I. Amoo, F. Asoore; "Effect of processing the nutrient composition and oil of peanut (Arachis hypogea) seed flour." *J. Chem. Soc. Nig., **31(1 & 2),** 1-5 (2006).*

[43] Ali, A., Khan, S., Hyder, S. and Nain, A. K; "Volumetric, viscometric and refractive index study of amino acids in mixed solvents at 308.15 K." *Phys. Chem. Liq., **44(6),** 655-62 (2006).*

[44] Husband, F. A., Garrood, M. J., Mackie, A. R., Burnett, G. R. and Wilde, P. J; "Adsorbed Protein Secondary and Tertiary Structures by Circular Dichroism and Infrared Spectroscopy with Refractive Index Matched Emulsions" *J. Agri. Food Chem., **49,** 859-66 (2001).*

[45] P. Ramasami, L. Jhaumeer, P. Rondeau, F. Cadet, H. Seepujak, A. Seeruttun; "Quantification of sugars in soft drinks and fruit juices by density, refractometry, infrared spectroscopy and statistical methods." *S. A. J. Chem., **57**, 24-27 (2004).*

[46] M. Godshall, E. Roberts, X. Miranda; "Composition of the soluble, nondialyzable components in raw cane sugar." *J. Food Proc. and Preser., **25(5),** 323-35 (2001).*

[47] V. A. Gunyakov, N. P. Shestakov and S. M. Shibli; "Density and refractive index measurements in hexaheptyloxytriphenylene, a discotic liquid crystal" *liq. Cry., **30(7),** 871–75 (2003)*.

[48] A. Dewaele, J. Eggert, P. Loubeyre, R. Le Toullec; "Measurement of refractive index and equation of state in dense He, H2, H2O, and Ne under high pressure in a diamond anvil cell." *Phy. Rev. B: Cond. Mat. Mater. Phy., **67(9),** 094112/1-8 (2003).*

[49] D. Leviton and P. Petrone; "Variations in refractive index of color filter glasses." *Proc. SPIE- Int. Soc. Opt. Eng., **3425**, 213-18 (1998).*

[50] R. Cisneros, C. Ramirez, C. Wang; "Ellipsometry and ab initio approaches to the refractive index of porous silicon." *J. Phy. : Cond. Mat.,* ***19(39),*** *395010/1-9 (2007).*

[51] G. Firanescu, R. Signorell; "Predicting the Influence of Shape, Size, and Internal Structure of CO Aerosol Particles on Their Infrared Spectra." *J. Phy. Chem. B.* ***113(18),*** *6366-77 (2009).*

[52] G. Lisa, L. Gabriela; "Prediction of excess thermodynamic properties from experimental refractive index of binary mixtures. 1. Water - propionic acid mixtures at 290.15, 300.15 and 310.15 K." *Rev. Roum. Chim.,* ***52(7),*** *647-53 (2007).*

[53] A. Mariano, M. Postigo, D. Gonzalez-Salgado, L. Romani; "Densities, speeds of sound, and refractive indices of the ternary mixtures (toluene + methyl acetate + butyl acetate) and (toluene + methyl acetate + methyl heptanoate) at 298.15 K." *J. Chem. Thermodyn.,* ***39(2),*** *218-24 (2007).*

[54] A. Ali, M. Tariq, F. Nabi; "Density, viscosity, refractive index, and speed of sound in binary mixtures of pyridine and 1-alkanols (C6, C7, C8, C10) at 303.15 K." *Chin. J. Chem.,* ***26(11),*** *2009-15 (2008).*

[55] J. Troncoso, E. Carballo, L. Romani; "Density and refractive index in mixtures of ionic liquids and organic solvents: Correlations and predictions." *J. Chem. Thermodyn.* ***40(6),*** *949-56 (2008).*

[56] R. Belda, J. Herraez and O. Diez; "A study of the refractive index and surface tension synergy of the binary water/ethanol: influence of concentration." *Phy. Chem. Liq.,* ***43(1),*** *91-101 (2005).*

[57] P. Miguel, C. Salvador and M. Alejandra; "Refractive and volumetric properties for binary liquid mixtures containing toluene and linear esters at 298.15 K." *J. Mol. Liqd.,* ***143(2-3)****, 115-18 (2008).*

[58] A. Ali, F. Nabi, M. Tariq; "Volumetric, viscometric, ultrasonic, and refractive index properties of liquid mixtures of benzene with industrially important monomers at different temperatures." *Int. J. Therm.,* ***30(2),*** *464-74 (2009)*.

[59] J. Liskowitz and J. Huang; "Measurement of the concentration of total dissolved solids, organic dissolved solids, and inorganic dissolved solids in the presence of suspended solids." *Water Qua. Instru.,* ***2,*** *100-9 (1974).*

[60] K. Sangwal, W. Kucharczyk; "Relationship between density and refractive index of inorganic solids." J. Phy. D: App. Phy., 20(4), 522-5 (1987).

[61] M. Taboada, G. Elisa; R. Hector and A. Teofilo; "Density, viscosity, refractive index and electrical conductivity of saturated solutions of the lithium hydroxide + ethanol + water system at 298.15 K, and thermodynamic description of the solid-liquid equilibrium." *Fluid Phase Equi.,* ***235(1),*** *104-11 (2005).*

[62] F. Li, M. Li, Q. Cui, T. Cui, Z. He, Q. Zhou and G. Zou; "The velocity, refractive index, and equation of state of liquid ammonia at high temperatures and high pressures." *J. Chem. Phy.,* ***131(13),*** *134502/1-5 (2009).*

[63] R. Brown, W. Boltin, B. Bandli, J. Millette; "Light and electron microscopy of mineral wool fibers." *Microscope,* ***55(1),*** *37-47(2007).*

[64] J. Cerna, A. Alejandro, M. Matla; "Analysis of the influence of glycidyl methacrylate on molecular weight and refractive index in styrene-methyl methacrylate-glycidyl methacrylate copolymers through mixture design of experiments." *J. App. Poly. Sci.,* ***114(3),*** *1935-41 (2009).*

[65] A. Soriano, B. Doma, H. Meng; "Measurements of the density and refractive index for 1-n-butyl-3-methylimidazolium-based ionic liquids." *J. Chem. Thermodyn.,* ***41(3),*** *301-07 (2009).*

[66] J. A. Riddick, W. B. Bunger and T. Sakano; Organic Solvents: Physical Properties and methods of purification, Fourth Edition., Techniques of Chemistry, II, A Wiley-Interscience Publication, John Wiley, New York (1986).

INTRODUCTION

Conductance is the ease with which current flows through a conductor. In solutions, ions conduct electricity so the conductance of such electrolytic solutions depends on the concentration of the ions and also on the nature of the ions present (through their charges and mobilities). The conductance behavior as a function of concentration is different for strong and weak electrolytes. Both strong and weak electrolytes have been studied over a wide range of concentrations [1-5].

Conductance measurements have been used for the determination of the equilibrium constants, degree of hydrolysis, dissociation constants, relative strength, basicity of organic acids, etc. Dutta studied aqueous solution of cellobiono-δ-lactone. Haberfield et al[6] used this technique to determine choline-anhydrocholine equilibrium. The relative strength of some disubstituted benzoic acids in different solvents at different temperature was studied by Mansour et al [9]. The conductometric method has also been used to study kinetics of reaction[10]. The conductance of solutions of various 1:1 electrolytes in N,N-dimethylacetamide have been measured by Das et al[11]. The dissociation constants of weak electrolytes have been reported by Kralj et al[8]. Peretrutov et al[12] have studied the aqueous solutions of zinc and copper tetra ammoniates. Recently, the technique is also used for the detection of microstructure of microemulsion[13]

Literature survey shows that conductance of many organic compounds, inorganic compounds, polymers, rare earth metals, amino acids, vitamins, ionic liquids, etc. have been measured[14-22]. Further, the conductivity measurements have been done in binary, ternary and quaternary liquid mixtures[23-30]. Many workers have been reported the conductance of organic synthetic compounds[31-37]. However, the conductivity data for cyanopyridines has not been reported but it is available for the complexes of various cyanopridines[38-39].

Thus, in the present section conductance of all the synthesized cyanopyridines was measured in DMF and DMSO solutions at 298.15 K, over a wide range of concentration.

EXPERIMENTAL

The solvents DMF and DMSO were purified by fractionally distillation by the method reported in the literature[40].

The solutions of different concentrations were prepared for each compound in DMF and DMSO and the conductance of each solution was measured by using Equip-tronics Conductivity Meter (Model No. 664) having cell constant 0.98 cm^{-1} at 298.15 K. The measured conductance was corrected by subtracting the conductance of pure solvent.

RESULTS AND DISCUSSION

The measured conductance (*k*) of each solution after correction was used to determine the specific conductance (κ), which is then used for the calculation of equivalent conductance (λ_c).

The equations used for calculating specific conductance (κ) and equivalent conductance (λ_c) are:

$$\kappa = k\theta \qquad \ldots (3.3.1)$$

$$\lambda_c = 1000\frac{\kappa}{C} \qquad \ldots (3.3.2)$$

where θ is the cell constant (= 0.98 cm^{-1}) and *c* is the concentration (g.equi./lit.) of solution.

Tables 3.3.1 and 3.3.2 show the equivalent conductance of all the studied compounds in DMF and DMSO solutions at 298.15 K along with measured conductance (*k*). The variation of conductance with concentration for these compounds in both the solvents is given in Figures 3.3.1 and 3.3.2. For the studied compounds, conductivities are observed to be less in DMSO than those in DMF. Further, for all the studied systems, conductance increases with concentration.

Figures 3.3.3 and 3.3.4 show the variation of equivalent conductance (λ_c) against $\sqrt{C}$ for all studied compounds in both DMF and DMSO solutions. It is observed that equivalent conductance increases with dilution. It is evident from these figures that all compounds behave as weak electrolytes. So, equivalent conductance at infinite dilution can not be evaluated by extrapolation for the studied systems.

Thus, it is concluded that in both DMF and DMSO solutions, the studied cyanopyridines exhibit weak electrolytic behavior.

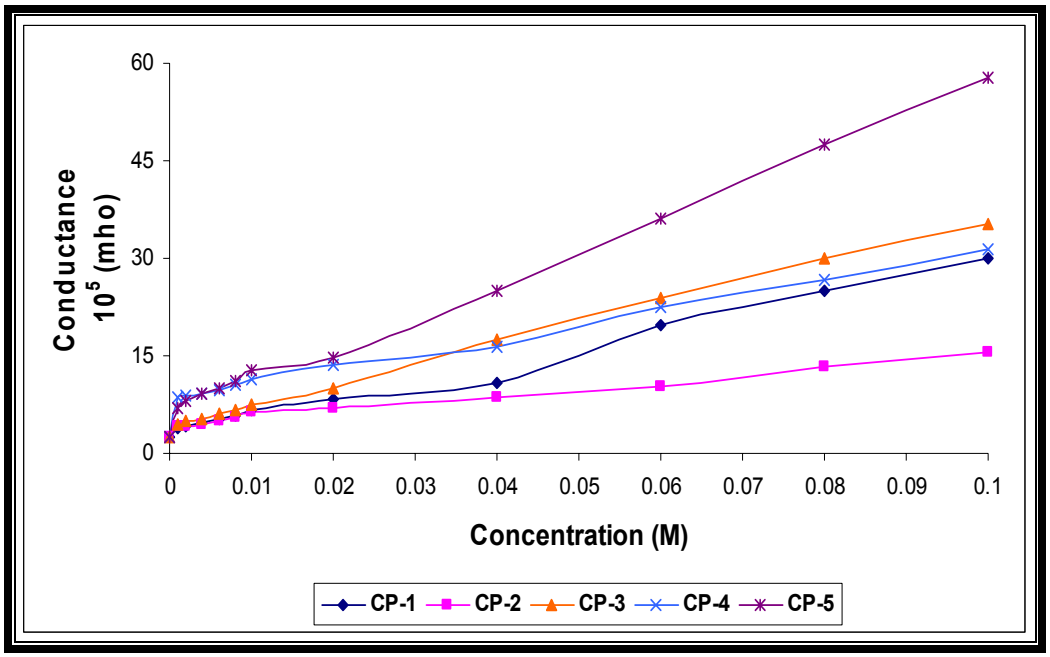
Table 3.3.1: The Conductance (*k*) and equivalent conductance (λ_C) of cyanopyridines in DMF at 298.15 K.

Conc. M	$k.10^5$ mho	λ_C mho.cm^2.equi.$^{-1}$	$k.10^5$ mho	λ_C mho.cm^2.equi.$^{-1}$	$k.10^5$ mho	λ_C mho.cm^2.equi.$^{-1}$	$k.10^5$ mho	λ_C mho.cm^2.equi.$^{-1}$	$k.10^5$ mho	λ_C mho.cm^2.equi.$^{-1}$
		CP-1		**CP-2**		**CP-3**		**CP-4**		**CP-5**
0.000	2.40	-	2.40	-	2.40	-	2.40	-	2.40	-
0.001	4.00	39.2000	4.10	40.1800	4.40	43.1200	8.50	83.3000	6.90	67.6200
0.002	4.30	21.0700	4.30	21.0700	4.90	24.0100	8.80	43.1200	8.10	39.6900
0.004	4.80	11.7600	4.50	11.0250	5.40	13.2300	9.30	22.7850	9.20	22.5400
0.006	5.30	8.6567	4.90	8.0033	6.00	9.8000	9.80	16.0067	9.90	16.1700
0.008	5.90	7.2275	5.60	6.8600	6.80	8.3300	10.50	12.8625	11.20	13.7200
0.010	6.80	6.6640	6.30	6.1740	7.60	7.4480	11.40	11.1720	12.80	12.5440
0.020	8.30	4.0670	7.00	3.4300	9.90	4.8510	13.70	6.7130	14.60	7.1540
0.040	10.80	2.6460	8.50	2.0825	17.50	4.2875	16.50	4.0425	24.90	6.1005
0.060	19.60	3.2013	10.30	1.6823	24.00	3.9200	22.50	3.6750	36.00	5.8800
0.080	25.00	3.0625	13.30	1.6293	29.90	3.6628	26.70	3.2708	47.40	5.8065
0.100	30.00	2.9400	15.50	1.5190	35.30	3.4594	31.50	3.0870	57.90	5.6742
		CP-6		**CP-7**		**CP-8**		**CP-9**		**CP-10**
0.001	5.60	54.8800	6.50	63.7000	8.40	82.3200	5.50	53.9000	4.50	44.1000
0.002	5.90	28.9100	6.80	33.3200	8.50	41.6500	5.80	28.4200	5.10	24.9900
0.004	6.90	16.9050	7.20	17.6400	8.70	21.3150	6.60	16.1700	5.70	13.9650
0.006	7.60	12.4133	8.00	13.0667	9.10	14.8633	7.30	11.9233	6.45	10.5350
0.008	9.50	11.6375	9.10	11.1475	9.50	11.6375	8.80	10.7800	7.90	9.6775
0.010	10.30	10.0940	10.60	10.3880	11.60	11.3680	9.90	9.7020	8.60	8.4280
0.020	14.20	6.9580	15.10	7.3990	12.80	6.2720	13.70	6.7130	11.10	5.4390
0.040	18.10	4.4345	28.30	6.9335	27.30	6.6885	17.90	4.3855	21.50	5.2675
0.060	21.70	3.5443	31.70	5.1777	35.10	5.7330	21.40	3.4953	29.70	4.8510
0.080	27.70	3.3933	38.30	4.6918	46.70	5.7208	27.80	3.4055	36.90	4.5203
0.100	35.00	3.4300	44.50	4.3610	53.00	5.1940	35.10	3.4398	43.10	4.2238

Table 3.3.2: The Conductance (*k*) and equivalent conductance (λ_C) of cyanopyridines in DMSO at 298.15 K.

Conc. M	$k.10^5$ mho	λ_C mho.cm^2.equi.$^{-1}$	$k.10^5$ mho	λ_C mho.cm^2.equi.$^{-1}$	$k.10^5$ mho	λ_C mho.cm^2.equi.$^{-1}$	$k.10^5$ mho	λ_C mho.cm^2.equi.$^{-1}$	$k.10^5$ mho	λ_C mho.cm^2.equi.$^{-1}$
	CP-1		**CP-2**		**CP-3**		**CP-4**		**CP-5**	
0.000	0.20	-	0.20	-	0.20	-	0.20	-	0.20	-
0.001	2.70	26.4600	2.50	24.5000	2.70	26.4600	3.50	34.3000	5.30	51.9400
0.002	2.90	14.2100	3.00	14.7000	3.70	18.1300	3.80	18.6200	5.60	27.4400
0.004	3.20	7.8400	3.10	7.5950	4.70	11.5150	4.20	10.2900	6.30	15.4350
0.006	3.70	6.0433	3.20	5.2267	5.10	8.3300	4.70	7.6767	7.40	12.0867
0.008	4.30	5.2675	3.30	4.0425	5.90	7.2275	5.30	6.4925	9.90	12.1275
0.010	5.10	4.9980	4.10	4.0180	6.90	6.7620	5.80	5.6840	11.20	10.9760
0.020	7.90	3.8710	5.60	2.7440	8.30	4.0670	6.20	3.0380	13.50	6.6150
0.040	9.50	2.3275	7.20	1.7640	9.80	2.4010	7.50	1.8375	15.90	3.8955
0.060	11.30	1.8457	8.30	1.3557	12.40	2.0253	9.70	1.5843	17.30	2.8257
0.080	13.60	1.6660	9.80	1.2005	14.80	1.8130	11.20	1.3720	19.60	2.4010
0.100	16.30	1.5974	12.00	1.1760	17.90	1.7542	13.90	1.3622	21.90	2.1462
	CP-6		**CP-7**		**CP-8**		**CP-9**		**CP-10**	
0.001	5.30	51.9400	6.30	61.7400	7.60	74.4800	5.10	49.9800	4.30	42.1400
0.002	5.50	26.9500	6.60	32.3400	7.90	38.7100	5.40	26.4600	4.90	24.0100
0.004	5.90	14.4550	7.20	17.6400	8.40	20.5800	5.90	14.4550	5.70	13.9650
0.006	6.50	10.6167	7.90	12.9033	9.10	14.8633	6.50	10.6167	6.50	10.6167
0.008	7.90	9.6775	8.80	10.7800	10.50	12.8625	7.80	9.5550	7.80	9.5550
0.010	9.30	9.1140	9.60	9.4080	12.10	11.8580	9.10	8.9180	9.60	9.4080
0.020	12.20	5.9780	11.70	5.7330	13.80	6.7620	12.70	6.2230	12.10	5.9290
0.040	14.10	3.4545	13.50	3.3075	15.10	3.6995	17.90	4.3855	21.50	5.2675
0.060	20.10	3.2830	15.70	2.5643	18.70	3.0543	21.40	3.4953	29.70	4.8510
0.080	25.70	3.1483	18.60	2.2785	20.70	2.5358	27.80	3.4055	36.90	4.5203
0.100	31.00	3.0380	20.50	2.0090	24.30	2.3814	34.10	3.3418	43.10	4.2238

Figure 3.3.1: The variation of conductance with concentration for cyanopyridines in DMF at 298.15 K.



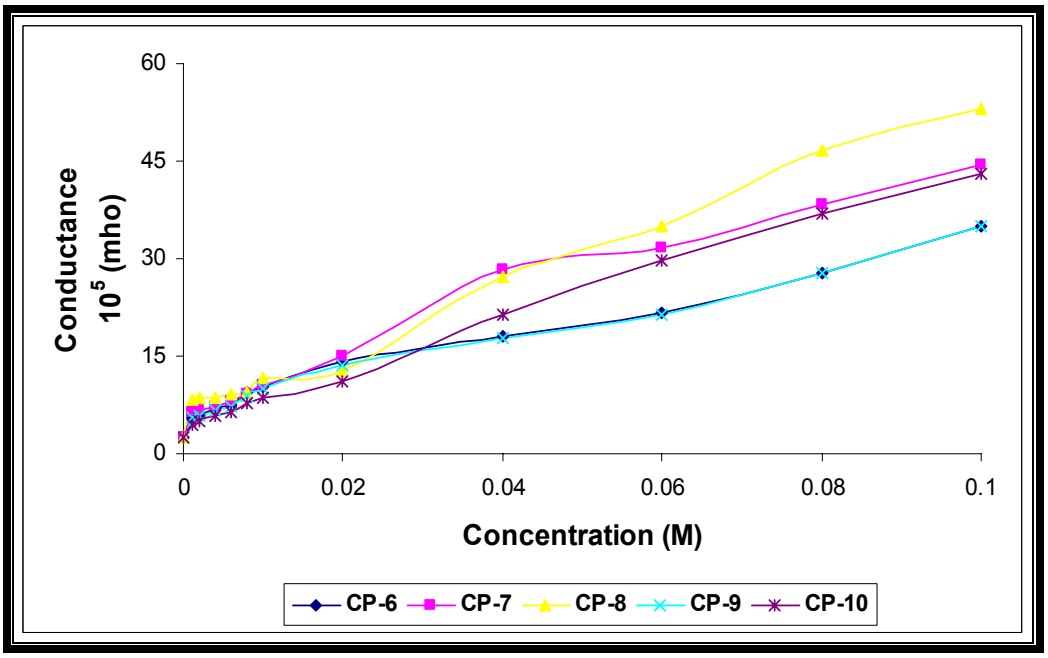
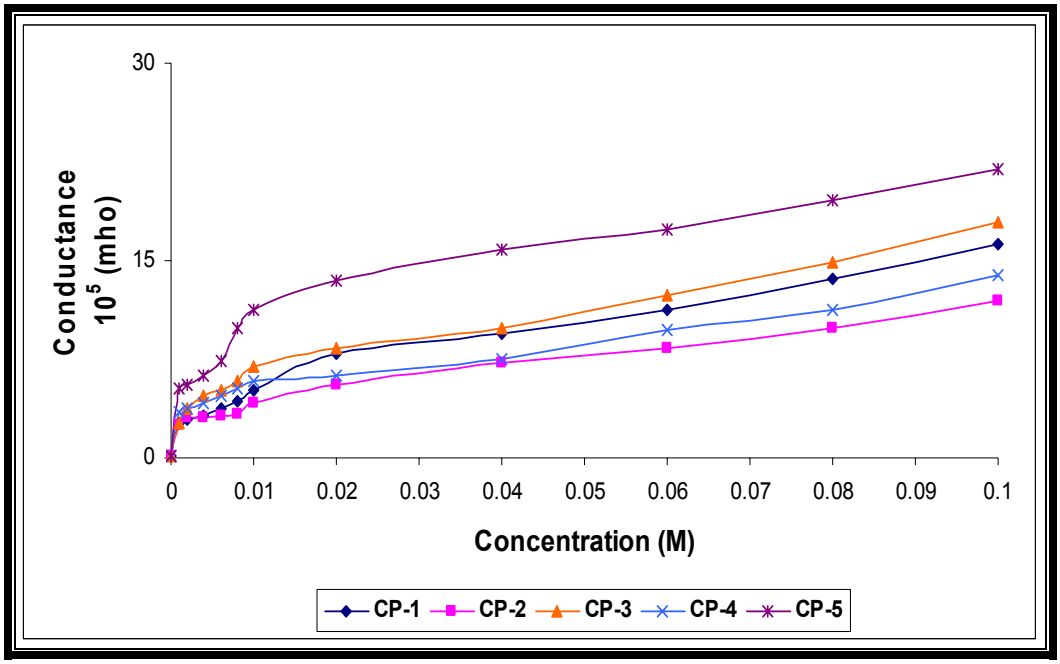


Figure 3.3.2: The variation of conductance with concentration for cyanopyridines in DMSO at 298.15 K.



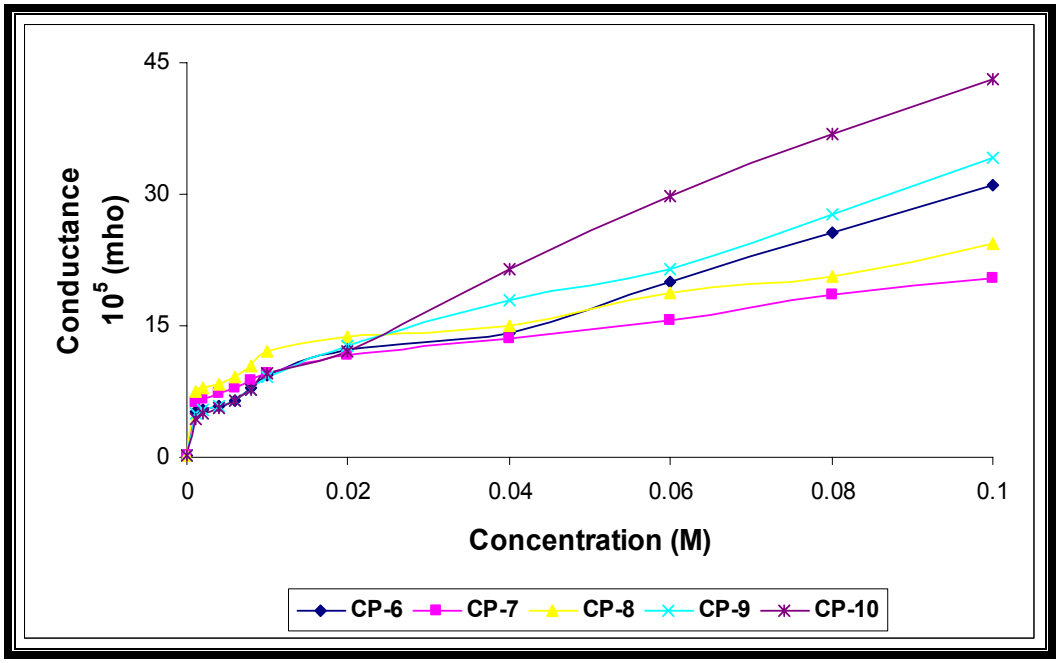
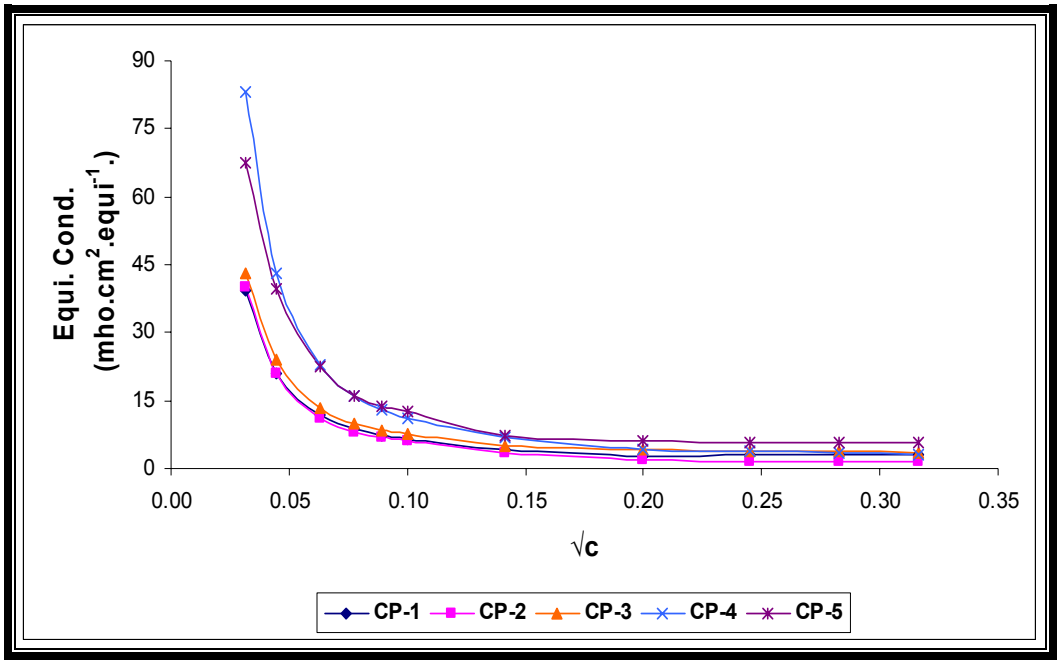


Figure 3.3.3: **The variation of equivalent conductance with √C for cyanopyridines in DMF at 298.15 K.**



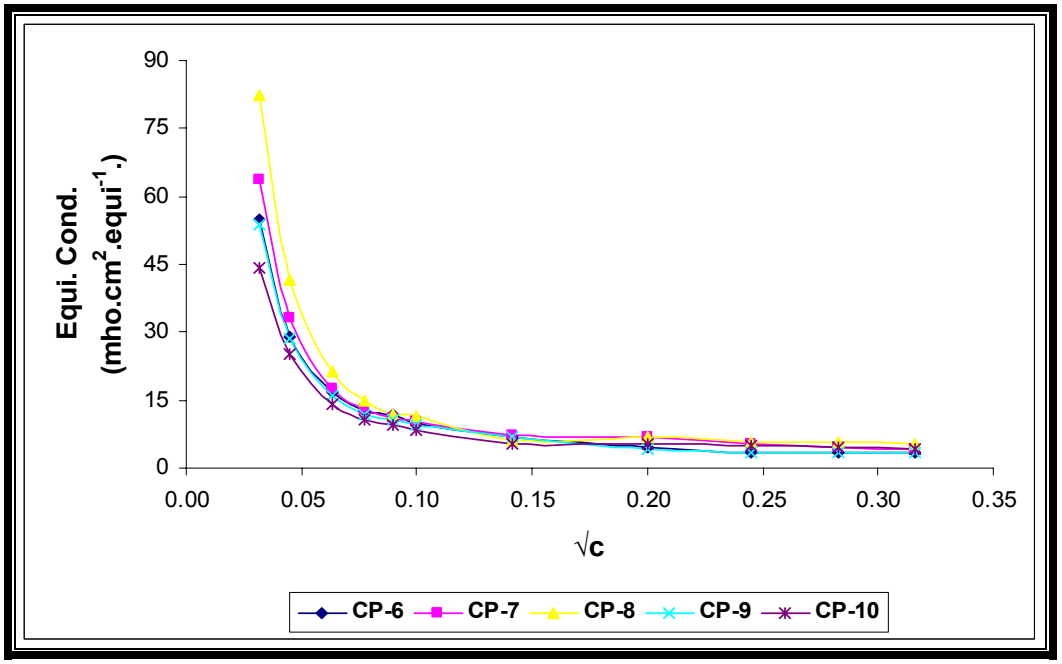
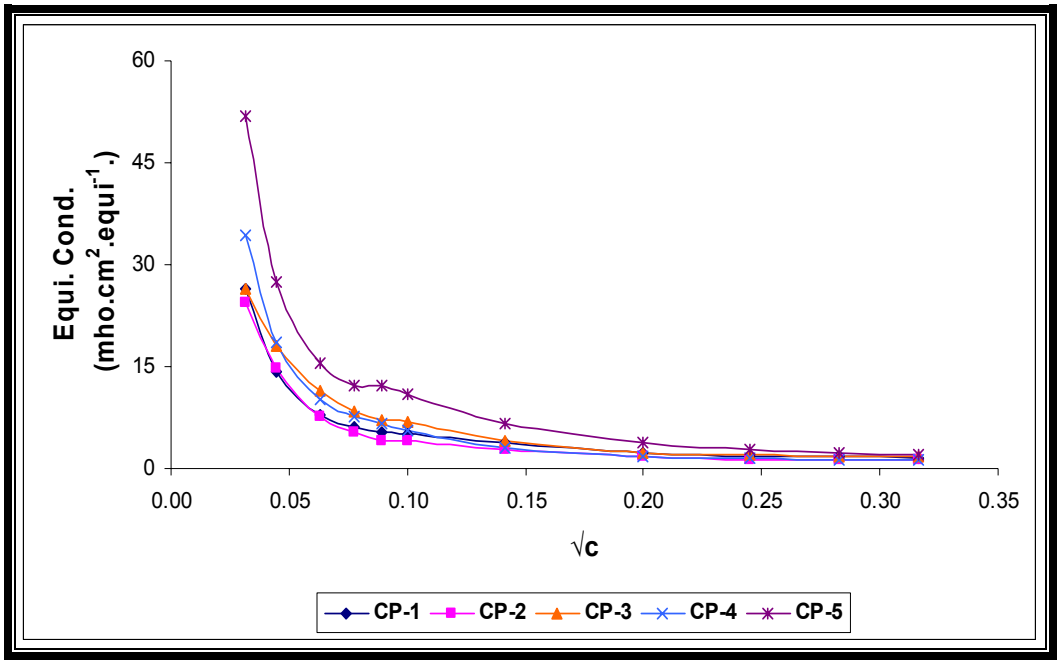
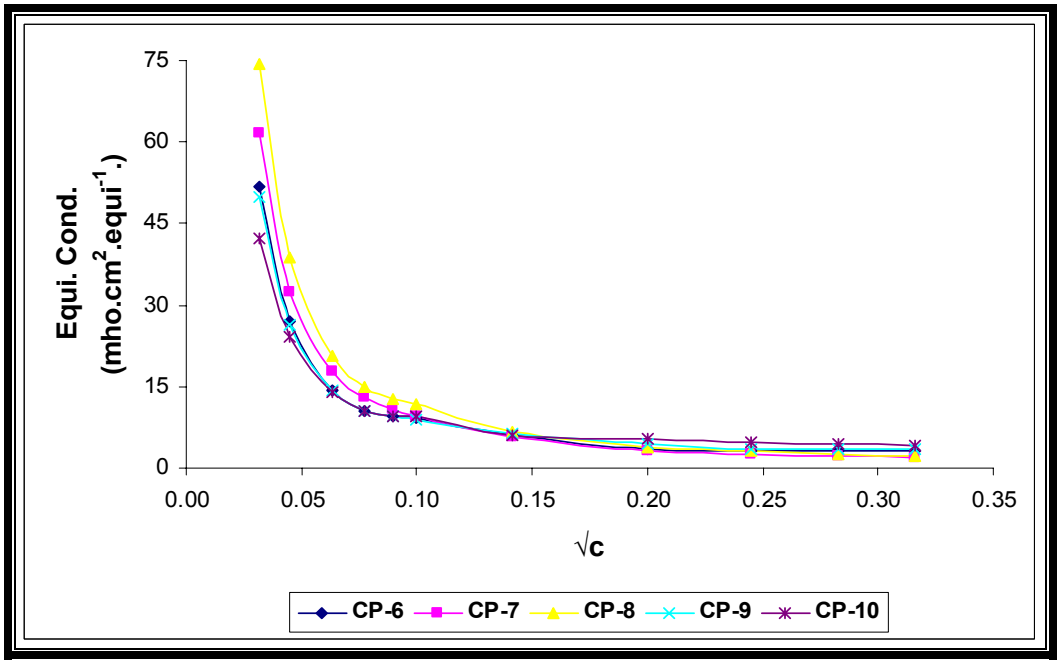


Figure 3.3.4: **The variation of equivalent conductance with √C for cyanopyridines in DMSO at 298.15 K.**





REFERENCES

[1] Barthel, J., Neueder, G. R. and Schmid, A; "Electrolyte solutions for technology-new aspects and approaches." *Pure Appl. Chem*., ***71,*** *1705-1715 (1999),*

[2] Barthel, J., Neueder, R., Feuerlein, F. and Iberl, L; "Conductance of electrolytes in ethanol solutions from-45 to 25 0C." *J. Sol. Chem., **12,** 449-471 (1983).*

[3] Barthel, J., Graml, H., Neueder, R., Turq, P. and Bernard, O; "Electrolyte conductivity from infinite dilution to saturation current topics in solution chemistry." *Res. Trends. (1994).*

[4] Falkenhagen, H. and Williams, J. W; "The frequency dependence of the electrical conductance of solutions of strong electrolytes." *J. Phy. Chem., **33,** 1121-1134 (1929).*

[5] Wang, K. and Sun, X; "A method for calculating thermal conductivity of electrolytic non-aqueous solutions." *Huaxue Gongcheng, **30,** 62-64 (2002).*

[6] Haberfield, P., Pessin, J. and Brooklyn C; "Proximate charge effects. 2. Enthalpies of solvent transfer in the choline-anhydrocholine equilibrium." *J. Ame. Chem. Soc., **104(23),** 6191-4 (1982).*

[7] Dutta, S. K; Preparation and study of certain aspects of aqueous solution chemistry of cellobiono-δ -lactone. *Ind. J. Chem., **13(2),** 192-3 (1975).*

[8] Kralj, Kovac A.; "Calculating the dissociation constant of weak electrolytes by measuring the conductivity." *Int. J. Nonlinear Sci., Num. Simul., **10(7),** 965-75 (2009).*

[9] Mansour, El S., Sayed M., Kassem, A.; "The relative strength of some disubstituted benzoic acids in different solvents and at different temperature." *J. Iraqi Chem. Soc., **12(1),** 261-80 (1987).*

[10] Deeble,D. J., Bothe, E., Heinz P., Parsons, B. J., Phillips, G., and Von S. C.; "The kinetics of hydroxyl-radical-induced strand breakage of hyaluronic acid. A pulse radiolysis study using conductometry and laser-light-scattering." Zeitschrift fuer Naturforschung, C: *J. Biosci., **45(9-10),** 1031-43 (1990).*

[11] Das, D., Das, B., Hazra, D. K.; "Conductance of Some 1:1 Electrolytes in N,N-Dimethylacetamide at 25°C." *J. Sol. Chem., **31(5),** 425-31 (2002).*

[12] Peretrutov, A. A., Chubenko, M. N., Kim, P. P.; "Physicochemical properties of eutonic aqueous solutions of zinc and copper tetraammoniates in the range 293-323 K." *Rus. J. Phy. Chem., A **83(10),** 1813-15 (2009).*

[13] Hu, A., Yao, Z., Yu, Xi.; "Phase behavior of a sodium dodecanol allyl sulfosuccinic diester/n-pentanol/methyl acrylate/butyl acrylate/water microemulsion system and preparation of acrylate latexes by microemulsion polymerization." *J. App. Poly. Sci., **113(4),** 2202-2208 (2009).*

[14] Rodriguez, A., Junquera, E., Patricia, A.; J. Collo. "Conductometric and spectrofluorimetric characterization of the mixed micelles constituted by dodecyltrimethylammonium bromide and a tricyclic antidepressant drug in aqueous solution." *Interface Sci., **269(2),** 476-83 (2004).*

[15] Clark, R. P., Goldsmith, H. J., and Blucher, R. L.; "Electrical conductance of the system LiCl-KCl-CaCrO4." *J. Chem. Eng. Data,* ***15(2),*** 277-80 (1970).

[16] Borah, P., Dutta, A.; "Conductivity study of some polymer electrolytes based on polyacrylonitrile*." Ionics,* ***15(6),*** *711-16 (2009).*

[17] Tsuji, T., Maeda, Y., Yamamura, Y.; "Electrical conductivity of MAl0.97Zn0.03O3-y (M=rare earth)." *J. Phy. Chem. Solids.,* ***66(2-4),*** *339-42 (2005).*

[18] Bobreshova, O. V., Polumestnaya, K. A., Fedosova, A. A.; "Ion-ion and ion-dipole interactions in acid and alkaline glycine solutions." *Rus. J. Electrochem.,* ***45(3),*** *345-349 (2009).*

[19] Hassan, N., Awad, S.; "Reverse effect of vitamin E on oxidative stress, derivatives and conductivity changes of hemoglobin induced by exposure to cadmium. "*J. App. Sci. Res.,* ***3(6),*** *437-43 (2007).*

[20] Ross, P. D., Scruggs, R. L., and Manning, G. S.; "Measurements and interpretation of the conductance of DNA in simple salt solutions." *Biopoly.,* ***14(9),*** *1991-3 (1975).*

[21] Malki, M., Echegut, P., Constantinescu, M., Olteanu, M.; "Electrical conductivity of glasses containing PbO in solid and molten state." Adv. Sci. Tech. (Faenza, Italy) Mass and Charge Trans. Inorg. Mat., ***37(2)*** 199-204 (2003).

[22] Stoppa, A., Johannes, H., and Buchner, R.; "Conductivities of Binary Mixtures of Ionic Liquids with Polar Solvents." *J. Chem. & Eng. Data,* ***54(2),*** *472-79 (2009) .*

[23] Rycerz, L., Ingier-Stocka, E., Gaune-Escard, M.; "Phase diagram and electrical conductivity of CeBr3-CsBr binary system." J. Thermal Ana. Cal., ***97(3),*** *1015-21 (2009).*

[24] Zhang, X., Hu, Y., Peng, X., Yue, W.; "Conductivities of Several Ternary Electrolyte Solutions and Their Binary Subsystems at 293.15, 298.15, and 303.15 K." *J. Sol. Chem.,* ***38(10),*** *1295-06 (2009).*

[25] Usobiaga, A., Diego, A., and Madariaga, J. M; "Electrical Conductivity of Concentrated H2TiF6 + HF + H2O Mixtures." *J. Chem. Eng. Data,* ***48(1),*** *81-85 (2003).*

[26] Satyanarayana, N., Patcheammalle, R., Muralidharan, P., Venkateswarlu, M.; "Synthesis by sol-gel route and electrical conductivity studies of the fast conducting silver based Ag2O-B2O3-SiO2 system." *Bul. Electrochem.*, ***12(11-12),*** *658-60 (1996).*

[27] Chen, H., Zhou, X., Woods, E. J., Gao, D.; "Electrical conductivity measurements for the ternary systems of glycerol/sodium chloride/water and ethylene glycol/sodium chloride/water and their applications in cryopreservation." *Biopreservation and Biobanking,* ***7(1),*** *13-7 (2009).*

[28] Sang, S., Yin, H., Deng, Miao,; "Metastable equilibria for the quaternary system Li2B4O7+Na2B4O7+K2B4O7+H2O at 15°C." *Chin. J. Chem.,* ***26(10),*** *1816-20 (2008).*

[29] Zuca, S., Olteanu, M., Borcan, R., Popescu, A. M., Ciochina, M.; "Electrical conductivity, density, and viscosity of molten magnesium chloride-calcium chloride-2-sodium chloride-potassium chloride quaternary system." *Chem. Papers,* ***45(5),*** *585-92 (1991).*

[30] Singh, A., Vishnu, K. S, Saket P.; "Conductance studies on the interaction of symmetrical tetraalkylammonium iodides with nonelectrolytes-sucrose and urea-in N,N-dimethylformamide." *Carbohydrate Res., **93(2),** 197-03 (1981).*

[31] Baluja, S.; "Physicochemical studies of some Schiff bases derived from 6-ethylbenzene-1, 3-diol." *E. J. Chem., **1,** 199-05 (2004).*

[32] Kabir-ud-Din, A. A., Mohammed, D. A., Naqvi, A. Z. and Akram, M.; "Conductometric study of antidepressant drug-cationic surfactant mixed micelles in aqueous solution, Colloids and Surfaces." *Biointerfaces, **64,** 65-69 (2008).*

[33] Parvatalu, P. and Srivastava. A. K. "Ionic Conductivity in Binary Solvent Mixtures. 6. Behavior of Selected 1:1 Electrolytes in 80 mass % Propylene Carbonate + p-Xylene at 25 °C." *J. Chem. Eng. Data, **48,** 608-11 (2003).*

[34] Campbell, T. G. and Urbach, F. L.; "Electronic, circular dichroism, and proton magnetic resonance spectral studies of the nickel(II) complexes of some neutral, tetradentate Schiff base ligands derived from 1,3-diamines." *Inorg. Chem., **12,** 1840-46 (1973).*

[35] Liu, J., Masuda, Y. and Sekido E. "A conductance study of macrocyclic Schiff base metal(II) complexes in methanol." *Bull. Chem. Soc. Jap., **63,** 2516-20 (1990).*

[36] Carlen, P. L., Gurevich, N. and Polc, P. "Low-dose benzodiazepine neuronal inhibition: enhanced Ca2+ mediated K+ conductance." *Brain res., 271, 358-64 (1983).*

[37] Baluja, S. Kasundra, P. and Vekariya, N. "Physicochemical studies of some azomethines of 5-amino isophthalic acid in solutions of DMF and DMSO at 308.15 K." *Int. J. Chem. Sci., **7,** 533-538 (2009).*

[38] Hassaan, Aly M. A., Khalifa, M. A., El-Gemeie, G. H., Mekheimer, R. A., Abdel Latif, R. M.; "Synthesis and characterization of complexes of cobalt(II), nickel(II), copper(II) and zinc(II) with 6-substituted 4-aryl-3-cyanopyridine-2-(1H)-thiones." *Sulfur Letters, **16(4),** 147-56 (1993).*

[39] Chang, James C., Haile, Marcus A. and Keith, Gary R.; "Cyanopyridine complexes of chromium(III)." *J. Inorg. Nuc. Chem., **34(1),** 360-2 (1972).*

[40] Riddick, J. A., Bunger, W. B. and Sakano, T.; "Organic Solvents-Physical Properties and methods of purification." Fourth Edition. Techniques of Chemistry, II, A Wiley-Interscience Publication, John Wiley, New York (1986).

INTRODUCTION

The extensive information on the thermodynamic properties of organic compounds is needed not only their use in many industrial processes but also for the advancement of theoretical developments through an understanding of the intermolecular forces[1] in solution for structure-property relationship[2,3]. Solubility data is important information in drug discovery, drug formulation[4] and crystallization-based separation investigations[5].

There are many methods for solubilization of drugs including cosolvency, surface active agents, salt information, complexation, hydrotropism, crystal engineering and preparation of soluble prodrug[6-8].

Solubility is a process which involves the breaking and making of bonds. The process of dissolution is accompanied by the heat change i.e., enthalpy change (ΔH_{sol}). If the heat is absorbed, the process is called endothermic. In this case, ΔH_{sol} is positive. If the heat is evolved i.e., process is exothermic and the ΔH_{sol} will be negative[9].

This enthalpy change is known as heat of solution, which is the change in heat content when one mole of substance is dissolved in specific quantity of solvent at a given temperature.

The molar heat of solution of a substance can be determined from the solubility measurement[10]. In recent years, various methods[11-18] have been used to study the solubility of natural compounds[19,20], organic compounds[21-23], polymers[24, 25], amino acids[26, 27], drugs[28-31], vitamins[32], ionic liquids[33,34], and inorganic compounds[35-37]. Alvarez et al. have reported the interactions between solvent molecules and nucleic acid by measuring the heat of solution[38]. The heat of solution of protein[39] has been studied by Randall et al. Quantitative relationship between solubility, initial dissolution rate and heat of solution of chiral drugs have also been reported by Yonemochi et al[40]. Further, the heat of solutions of some heterocyclic compounds have also been reported[41,43] In our laboratory, heat of solution of some synthesized heterocyclic compounds and drugs has also been determined[44-46]. Further, some thermodynamic parameters have also been evaluated from solubility data.

In the present section, the solubility for some synthesized cyanopyridine derivatives was determined in N, N-dimethylformamide (DMF) and

dimethylsulfoxide (DMSO) at different temperatures (298.15 to 318.15) K. Further, some thermodynamic parameters such as enthalpy, Gibb's energy and entropy of different solutions have also been evaluated from the solubility data.

EXPERIMENTAL

For the solubility measurements, DMF and DMSO solvents were used which were purified by the method reported in the literature[47].

The solubility was measured by a gravimetric method[48]. For each measurement, an excess mass of synthesized cyanopyridine derivative was added to a known mass of solvent. Then, the equilibrium cell was heated to a constant temperature with continuous stirring. After, at least 3 h (the temperature of the water bath approached constant value, then the actual value of the temperature was recorded), the stirring was stopped and the solution was kept still for 2 h. A portion of this solution was filtered and by a preheated injector, 2 ml of this clear solution was taken in another weighted measuring vial (m_0). The vial was quickly and tightly closed and weighted (m_1) to determine the mass of the sample (m_1- m_0). Then, the vial was covered with a piece of filter paper to prevent dust contamination. Then, the vial was placed in at room temperature to evaporate the solvent. After the solvent in the vial had completely evaporated, the vial was dried and reweighed (m_2) to determine the mass of the constant residue solid (m_2- m_0). All the weights were taken using an electronic balance (Mettler Toledo AB204-S, Switzerland) with an accuracy of ± 0.0001 g. Thus, the solid concentration of the sample solution of mole fraction, x, could be determined from equation 3.4.1

$$x = \frac{(m_2 - m_0)/M_1}{(m_2 - m_0)/M_1 + (m_1 - m_2)/M_2} \qquad .. (3.4.1)$$

where M_1 is the molar mass of cyanopyridine derivative and M_2 is the molar mass of the solvent.

RESULTS AND DISCUSSION

The solubility or mole fraction solubility *(x)* of synthesized compounds in the studied solvents is given in Tables 3.4.1 and 3.4.2. It is evident from these Tables that the solubility increases with temperature in both the solvents. Figure

3.4.1 shows the variation of mole fraction solubility (x) against temperature for CP-1 in DMF and DMSO. Comparison of solubility of these compounds in DMF and DMSO shows that overall solubility is greater in DMSO than that in DMF. The dielectric constant and dipole moment of DMSO (46.6, 3.9) are greater than that of DMF (36.71, 3.86). Thus, these properties of solvent play an important role on the solubility, as expected.

The temperature dependence solubility in solvents is described by the modified Apelblat equation[49, 50]

$$\ln x = A + B(T/K) \qquad \text{..... (3.4.2)}$$

where x is the mole fraction solubility of compounds; T is the absolute temperature and A, and B are the coefficients. The values of these coefficients are given in Table 3.4.3. Using these values of A and B, calculated solubilities x_c were evaluated and are reported in Tables 3.4.1 and 3.4.2.

The relative deviations *(RD)* between the experimental and calculated values of solubilities are also calculated by equation 3.4.3 and are given in Tables 3.4.1 and 3.4.2.

$$\textit{Relative Deviation} = \left(\frac{x - x_c}{x} \right) \qquad \text{..... (3.4.3)}$$

Further, relative average deviations *(ARD)* and root-mean-square deviations *(rmsd)* were calculated by equations 3.4.4 and 3.4.5 and are listed in Tables 3.4.5 and 3.4.6.

$$ARD = \frac{1}{N} \sum_{i}^{N} \left(\frac{x_i - x_c}{x_i} \right) \qquad \text{..... (3.4.4)}$$

$$rmsd = \left[\sum_{i=1}^{N} \frac{(x_{ci} - x_i)^2}{N-1} \right]^{1/2} \qquad \text{..... (3.4.5)}$$

where N is the number of experimental points.

Table 3.4.1: The experimental solubility *(x),* calculated solubility *(x_c)* and relative deviation *(RD)* of cyanopyridines derivatives in DMF at different temperatures.

Temp. K	*x*	*x_c*	*100 RD*	*x*	*x_c*	*100 RD*
	CP-1			*CP-6*		

298.15	0.0049	0.0044	-0.0096	0.0081	0.0080	-0.0021
303.15	0.0050	0.0056	0.0109	0.0092	0.0092	-0.0002
308.15	0.0069	0.0071	0.0060	0.0103	0.0105	0.0057
313.15	0.0095	0.0092	-0.0073	0.0121	0.0120	-0.0016
318.15	0.0122	0.0117	-0.0107	0.0139	0.0138	-0.0033
	CP-2			***CP-7***		
298.15	0.0044	0.0045	0.0026	0.0040	0.0042	0.0038
303.15	0.0054	0.0053	-0.0018	0.0055	0.0053	-0.0038
308.15	0.0063	0.0062	-0.0031	0.0071	0.0067	-0.0080
313.15	0.0073	0.0072	-0.0018	0.0086	0.0084	-0.0046
318.15	0.0082	0.0084	0.0050	0.0101	0.0105	0.0100
	CP-3			***CP-8***		
298.15	0.0065	0.0067	0.0045	0.0074	0.0079	0.0103
303.15	0.0081	0.0079	-0.0049	0.0094	0.0093	-0.0031
308.15	0.0098	0.0092	-0.0122	0.0115	0.0109	-0.0138
313.15	0.0111	0.0108	-0.0060	0.0128	0.0128	-0.0007
318.15	0.0123	0.0127	0.0088	0.0141	0.0150	0.0207
	CP-4			***CP-9***		
298.15	0.0049	0.0050	0.0018	0.0086	0.0088	0.0031
303.15	0.0061	0.0059	-0.0031	0.0104	0.0102	-0.0054
308.15	0.0072	0.0071	-0.0036	0.0121	0.0117	-0.0089
313.15	0.0086	0.0084	-0.0039	0.0138	0.0136	-0.0058
318.15	0.0099	0.0100	0.0034	0.0155	0.0157	0.0048
	CP-5			***CP-10***		
298.15	0.0080	0.0085	0.0093	0.0075	0.0079	0.0075
303.15	0.0101	0.0098	-0.0066	0.0095	0.0092	-0.0064
308.15	0.0123	0.0113	-0.0215	0.0116	0.0108	-0.0179
313.15	0.0133	0.0131	-0.0057	0.0129	0.0126	-0.0061
318.15	0.0144	0.0151	0.0166	0.0142	0.0148	0.0142

Table 3.4.2: The experimental solubility *(x)*, calculated solubility *(x_c)* and relative deviation *(RD)* of cyanopyridine derivatives in DMSO at different temperatures.

Temp. K	***x***	***X_c***	***100 RD***	***x***	***x_c***	***100 RD***

	CP-1			***CP-6***		
298.15	0.0049	0.0049	0.0004	0.0082	0.0082	-0.0005
303.15	0.0063	0.0063	-0.0004	0.0095	0.0094	-0.0024
308.15	0.0077	0.0081	0.0075	0.0108	0.0108	-0.0004
313.15	0.0104	0.0103	-0.0017	0.0125	0.0123	-0.0041
318.15	0.0131	0.0132	0.0021	0.0142	0.0141	-0.0008
	CP-2			***CP-7***		
298.15	0.0060	0.0060	-0.0005	0.0045	0.0046	0.0032
303.15	0.0066	0.0065	-0.0012	0.0059	0.0057	-0.0041
308.15	0.0071	0.0071	0.0010	0.0074	0.0070	-0.0086
313.15	0.0078	0.0078	0.0000	0.0088	0.0086	-0.0045
318.15	0.0086	0.0085	-0.0016	0.0102	0.0106	0.0071
	CP-3			***CP-8***		
298.15	0.0066	0.0067	0.0031	0.0076	0.0080	0.0098
303.15	0.0081	0.0080	-0.0030	0.0096	0.0093	-0.0065
308.15	0.0097	0.0094	-0.0067	0.0115	0.0108	-0.0176
313.15	0.0113	0.0111	-0.0043	0.0126	0.0124	-0.0039
318.15	0.0128	0.0131	0.0066	0.0136	0.0144	0.0170
	CP-4			***CP-9***		
298.15	0.0050	0.0054	0.0061	0.0085	0.0088	0.0067
303.15	0.0064	0.0062	-0.0031	0.0104	0.0102	-0.0035
308.15	0.0078	0.0073	-0.0105	0.0122	0.0119	-0.0084
313.15	0.0085	0.0084	-0.0011	0.0138	0.0137	-0.0015
318.15	0.0093	0.0098	0.0108	0.0154	0.0159	0.0119
	CP-5			***CP-10***		
298.15	0.0081	0.0086	0.0105	0.0075	0.0078	0.0068
303.15	0.0102	0.0100	-0.0047	0.0090	0.0089	-0.0032
308.15	0.0122	0.0115	-0.0152	0.0106	0.0100	-0.0129
313.15	0.0134	0.0133	-0.0023	0.0114	0.0113	-0.0031
318.15	0.0146	0.0154	0.0188	0.0122	0.0127	0.0116

Table 3.4.3: Coefficients *A* and *B* of equation 3.4.2, relative average deviation *(ARD)* and root mean square deviation *(rmsd)* of cyanopyridine derivatives in DMF and DMSO.

Compounds	***A***	***B***	***10^7 rmsd***	***100 ARD***
		DMF		

CP-1	-20.226	0.0496	0.82	-0.0021
CP-2	-14.547	0.0307	0.09	0.0002
CP-3	-14.547	0.0320	0.51	-0.0020
CP-4	-15.676	0.0348	0.09	-0.0011
Cp-5	-13.327	0.0287	1.39	-0.0016
CP-6	-12.845	0.0269	0.08	-0.0003
CP-7	-19.125	0.0458	0.39	-0.0005
CP-8	-14.445	0.0322	1.15	0.0027
CP-9	-13.352	0.0289	0.27	-0.0024
CP-10	-14.299	0.0317	1.04	-0.0017
DMSO				
CP-1	-20.138	0.0497	0.11	0.0016
CP-2	-10.366	0.0176	0.01	-0.0004
CP-3	-14.960	0.0334	0.20	-0.0009
CP-4	-14.232	0.0302	0.51	0.0004
Cp-5	-13.308	0.0287	1.11	0.0014
CP-6	-12.915	0.0272	0.03	-0.0017
CP-7	-17.660	0.0412	0.32	-0.0014
CP-8	-13.470	0.0290	1.20	-0.0002
CP-9	-13.495	0.0294	0.41	0.0010
CP-10	-12.034	0.0241	0.60	-0.0001

These values suggest that there is good agreement between experimental and calculated solubility values. So, the modified Apelblat equation can be used as model for the evaluation of solubility of these compounds in different solvents.

According to van't Hoff analysis, the standard enthalpy change of solution is obtained from the slope the *ln x* versus *1/T* plot. However, in recent thermodynamic treatments, some modifications have been introduced in the

van't Hoff equation to diminish the propagation of errors and consequently to separate the chemical effects from those due to statistical treatment used when enthalpy-entropy compensation plots are developed[51]. For this reason, the mean harmonic temperature (T_{hm}) is used in the van't Hoff analysis, which is calculated by the following equation.

$$T_{hm} = \frac{n}{\sum_{i}^{n}\left(1/T\right)} \qquad \text{..... (3.4.6)}$$

where n is the number of temperatures studied and T is absolute temperature of the experiment. In the present case, the T_{hm} value obtained is 308 K.

So, the modified van't Hoff equation is[52, 53].

$$\frac{\partial \ln x}{\partial\left(1/T - 1/T_{hm}\right)_{P}} = -\frac{\Delta H_{sol}}{R} \qquad \text{..... (3.4.7)}$$

where ΔH_{sol} is the heat of solution and R is the gas constant.

Figure 3.4.2 shows the van't Hoff plots for CP-1 in DMF and DMSO solutions. The slope of these linear plots gives the values of ΔH_{sol} whereas Gibb's energy of dissolution (ΔG_{sol}) was evaluated from the intercept using the following equation[52].

$$\Delta G_{sol} = -RT_{hm}.\ intercept \qquad \text{..... (3.4.8)}$$

Using these evaluated ΔH_{sol} and ΔG_{sol} values, the entropies of solutions (ΔS_{sol}) were obtained from the following equation[54]

$$\Delta S_{sol} = \frac{\Delta H_{sol} - \Delta G_{sol}}{T_{hm}} \qquad \text{..... (3.4.9)}$$

All these thermodynamic parameters are given in Table 3.4.4.

Figure 3.4.1: The mole fraction solubility (x) against temperature (T) for CP-1 in [A] DMF and [B] DMSO.

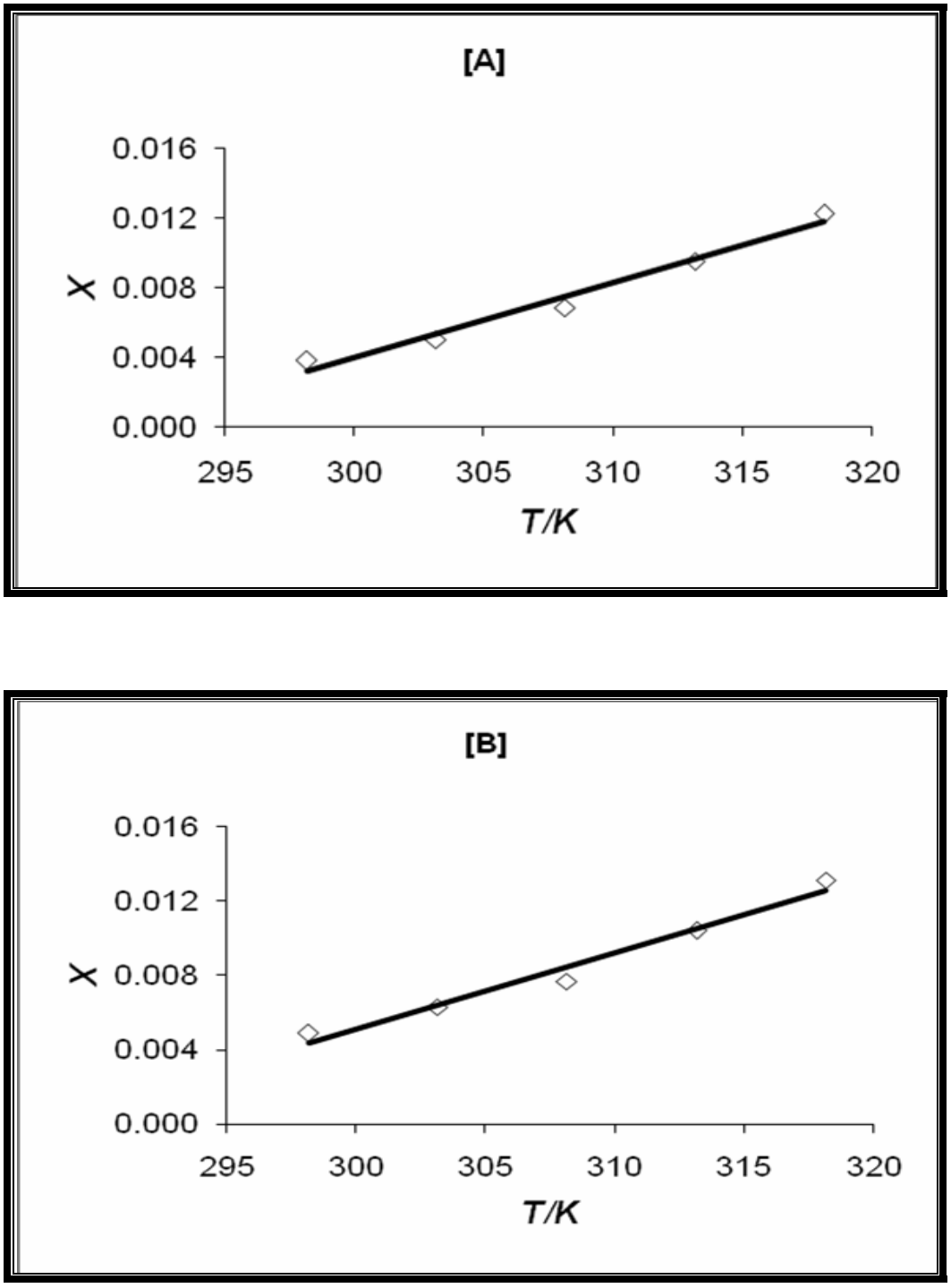
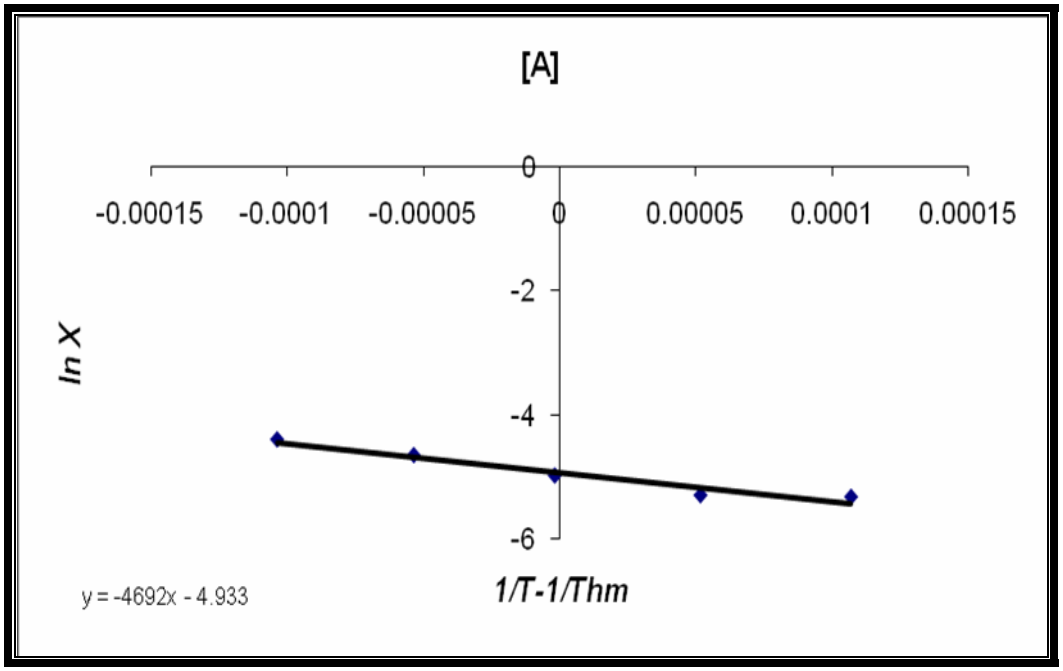


Figure 3.4.2: van't Hoff plots for CP-1 in [A] DMF and [B] DMSO.



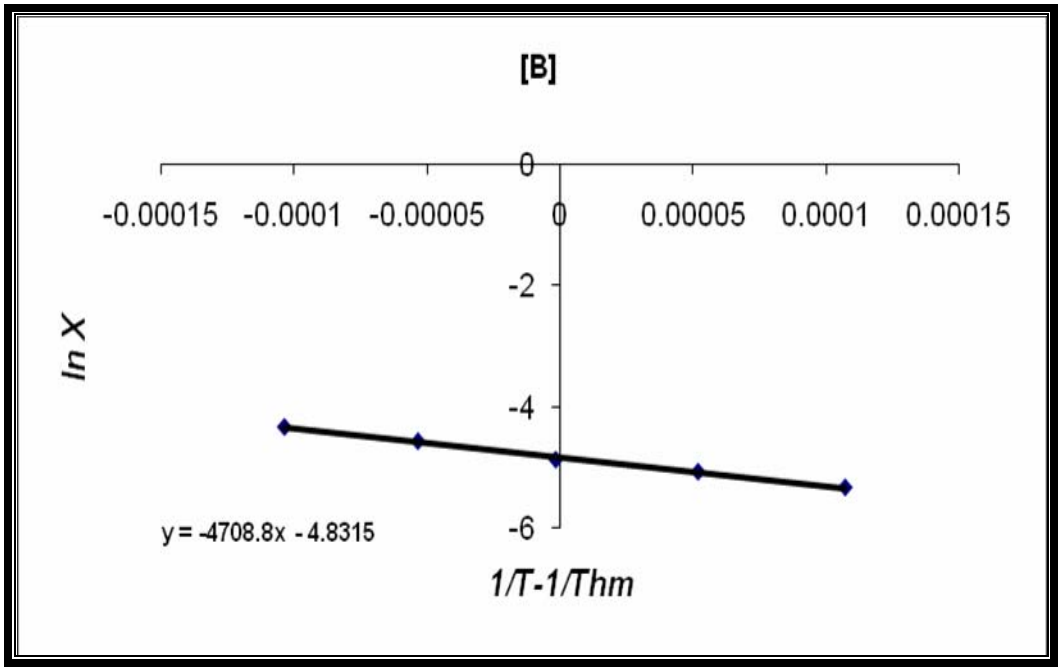


Table 3.4.4: The thermodynamic function of cyanopyridines derivatives in DMF and DMSO solutions at 308 K *(T_{hm}).*

Compound code	ΔH_{sol} kJ.mol^{-1}	ΔG_{sol} kJ.mol^{-1}	ΔS_{sol} J.mol^{-1}.K^{-1}	ΔH_{sol} kJ.mol^{-1}	ΔG_{sol} kJ.mol^{-1}	ΔS_{sol} J.mol^{-1}.K^{-1}
	DMF			DMSO		
CP-1	39.01	12.63	85.64	39.15	12.37	86.94
CP-2	24.25	13.02	36.47	13.88	12.65	4.00
CP-3	25.33	11.97	43.38	26.40	11.94	46.94
CP-4	27.50	12.65	48.19	23.91	12.62	36.65
Cp-5	22.75	11.46	36.65	22.71	11.44	36.58
CP-6	21.18	11.66	30.93	21.47	11.59	32.08
CP-7	36.22	12.81	75.98	32.59	12.68	64.64
CP-8	25.46	11.60	44.98	22.98	11.61	36.91
CP-9	22.85	11.36	37.32	23.23	11.36	38.52
CP-10	25.11	11.58	43.92	19.08	11.80	23.66

It is evident from Table 3.4.4 that for all the compounds ΔH_{sol}, ΔG_{sol} and ΔS_{sol} values are positive for both the solvents. When stronger bonds are broken and weaker bonds are formed, energy is consumed and so, ΔH_{sol} becomes

positive[54]. This indicates endothermic dissolution of compounds where the enthalpy term contributes to an unfavorable positive value of ΔG_{sol} [54]. Thus, positive values of ΔG_{sol} indicate that the dissolution process is not spontaneous[54, 55]. The positive value of entropy (ΔS_{sol}) indicates randomness in solutions[54].

REFERENCES

[1] E. Pedemonte and L. Lanzavecchia; "Compatible polymer mixtures. Evaluation of the interaction parameter from heat of solution measurements." *J. Calorimet. Anal. Thermiq. Thermodyn.Chim., **17**, 519-21, (1986).*

[2] P. Berti, S. Cabani, G. Conti, V. Mollica; "Thermodynamic study of organic compounds in octan-1-ol. 2. Enthalpy changes in the transfer of primary, secondary, and tertiary amines from gas and the dilute aqueous state." *Thermochim. Acta, **122(1)**, 1-8, (1987).*

[3] K. Masato, S. Toshiya and K. Hirofumi; "Enthalpy−entropy compensation for enantio−separation on cellulose and amylose tris (3, 5−dimethylphenylcarbamate) derivatives as stationary phases."*Chromatography, **24(3)**, 121-25, (2003).*

[4] A. Shayanfar, S. Soltanpour, F. Jabbaribar, A. Hamidi, W. Acree, A. Jouyban; "Solubility of Anthracene in quaternary solvent mixtures of 2,2,4-Trimethyl pentane + 2-Propanone + Methanol + Alcohols at 298.15 K." *J. Chem. Eng. Dtata, **53**, 2250–53, (2008).*

[5] J. Nti-Gyabaah, R. Chmielowski, V. Chan, Y. Chiew; "Solubility of Lovastatin in a family of six Alcohols: Ethanol, 1-Propanol, 1-Butanol, 1-Pentanol, 1-Hexanol and 1-Octanol." *Int. J. Pharm., **359**, 111-17,(2008).*

[6] Q. Niea, J. Wang; "Solubility of 16, 17-Epoxyprogesterone in six different solvents." *J. Chem. Eng. Data, **50,** 1750-52, (2005).*

[7] J. Elder; "Thermal behavior of Lovastatin." *Thermochem. Acta., **134,** 41-5, (1998).*

[8] G. Ren and J. Wang; "Solubility of DL-p-hydroxyphenylglycine sulfate in binary acetone + water solvent mixtures." *J. Chem. Eng. Data, **49,** 1376-78, (2004).*

[9] J. Chickos, W. Acree, J. Liebman; "Estimating solid-liquid phase change enthalpies and entropies." *J. Phy. Chem. Ref. Data, **28(6)**, 1535-73, (1999).*

[10] G. Samuel; "Thermodynemics for Chemist", *Litton Edu. Pub., Inc., New York, (1946).*

[11] M. Enrique, L. Jose, "Polymer Solubility Parameters of Poly (propylene oxide) Rubber from Inverse Gas Chromatography Measurements" *Poly. J., **28,** 127-30, (1996).*

[12] G. Price, I. Shillcock, "Inverse gas chromatographic measurement of solubility parameters in liquid crystalline systems." *J. Chromato., **964(A),** 199-204, (2002).*

[13] G. Hou, Q. Yin, Y. Yang, Y. Hu, M. Zhang, J. Wang; "Solubilities of adefovir dipivoxil in different binary solvents at 298.15 K." *J. Chem. Eng. Data.,**53,** 1021–23, (2008).*

[14] S. Kanji, and T. Masahiro; "Solubility control by UV irradiation of a copolymer having both photobase generating groups and photoacid generating groups" *Chem. Commun., 853-854, (1997).*

[15] H. Bettina, G. Sabine, A. Michael, S. Christoph; "Comparison of Nephelometric, UV-Spectroscopic and HPLC Methods for High-Throughput Determination of Aqueous Drug Solubility in Microtiter Plates." *Anal. Chem., **81**, 3165–72, (2009).*

[16] N. Jaroslav; "Solid-Liquid Phase Equilibria" *Elsevier Sci. Pub.Co. New York, (1977)..*

[17] P. Ma, Q. Xia; "Determination and Correlation for Solubility of Aromatic Acids in Solvents." *Chin. J. Chem. Eng., **9,** 39–44, (2001).*

[18] D. Wei, Y. Pei; "Measurement and correlation of solubility of diphenyl carbonate in alkanols." *Ind. Eng. Chem. Res., **47,** 8953–56, (2008).*

[19] L. Fatima, J. Antonio, P. Simao, A. Eugenia; "Aqueous Solubility of Some Natural Phenolic Compounds." *Ind. Eng. Chem. Res., **47,** 5182–89, (2008).*

[20] E. Sashina, A. Bochek, N. Novoselov, D. Kirichenko; "Structure and Solubility of Natural Silk Fibroin." *Russ. J. Appl. Chem., **79**, 869-876, (2006).*

[21] A. Daneshfar, H. Ghaziaskar, N. Homayoun; "Solubility of Gallic acid in Methanol, Ethanol, Water and Ethyl Acetate." *J. Chem. Eng. Data., **53**, 776-78, (2008).*

[22] A. Shalmashi, A. Eliassi; "Solubility of L-(+)-Ascorbic Acid in Water, Ethanol, Metanol, Propan-2-ol, Acetone, Acetonitrile, Ethyl Acetate and Tetrahydrofuran from (293 to 323) K" *J. Chem. Eng. Data., **53**, 1332-34, (2008).*

[23] E. Voutsas, E. Panteli; "Solubilities of Cinnamic Acid Esters in Ionic liquids" *J. Chem. Eng. Data., **54,** 812-18, (2009).*

[24] H. Yuichi, D. Violette; "Effect of temperature on the solubility of aroma compounds in polyethylene film" *Poly. Test.,**25,** 690-96, (2006).*

[25] G. Mansoori, A. Eliassi, H. Modarress; "Measurement of Activity of water in aqueous Poly(ethylene glycol)Solutions (Effect of Excess Volume on the Flory-Huggins χ-Parameters)." *J. Chem. Eng. Data., **44**, 52-55, (1999).*

[26] A. Pradhan, J. Vera; "Effect of acids and bases on the solubility of amino acids". *Fluid Phase Equi., **152**, 121-32, (1998).*

[27] E. Macedo; "Solubility of amino acids, sugars, and proteins" *Pure Appl. Chem., 77, 559–68, (2005).*

[28] C. Zhou, M. Kong, X. Shi, Y. Cao; "Solubility of Imidaclopride in different solvents" *J. Chem. Eng. Data., **53**, 615–18, (2008).*

[29] A. Jouyban, W. Acree, M.Fakhree, A. Shayanfar; "Solubility of Lamotrigine, Diazepam and Clonazepam in Ethanol + Water mixtures at 298.15K." *J. Chem. Eng. Data.,**54,** 1107-09, (2009).*

[30] Q. Yin, K. Guo, M. Zhang, J. Wang; "Solubility of Losartan Potassium in different binary solvents from (293.15 to 343.15) K". *J. Chem. Eng. Data, **53**, 1138-40, (2008).*

[31] Q. Ren, W. Chen, B. Su, H. Xing, Y. Yang; "Solubility of Demosterol in five organic solvents." *J. Chem. Eng. Data., **53,** 2715-17, (2008).*

[32] D. Michael and R Gupta; "Solubility of Vitamin E (r-Tocopherol) and Vitamin K3 (Menadione) in Ethanol–Water Mixture." *J. Chem. Eng. Data, **43**, 590-91, (1998)*

[33] W. James, L. Kristina, P. Mark, M. Markus; "Surprisingly high solubility of the ionic liquid trihexyltetradecylphosphonium chloride in dense carbon dioxide" *Green Chem., **7,** 475–78, (2005).*

[34] K. Takashi; "Mutual Solubility of Hydrophobic Ionic Liquids and Water in Liquid-Liquid Two-phase Systems for Analytical Chemistry". Anal. Sci., ***24,*** 1221-30, (2008).

[35] A. Kumar, J. Shukla, V. Mohandas; "Effect of pH on the Solubility of CaSO4.2H2O in Aquious NaCl solutions and physicochemical solution properties at 35 0C" *J. Chem. Eng. Data, **53,** 2797-2800, (2008).*

[36] F. Buryukin, V. Tverdokhlebov, V. Fedorov, E. Tetenkova, A. Fedorova and O. Azanova; "The Solubility of Acetylferocene and Diacetylferocene in dimethylsulfoxide and its mixtures with water" *Russ. J. Phy. Chem., **82(A)**, 1545-48, (2008).*

[37] W. Yan, L. Dang, Z. Wei, H. Wei; "Solubility of Ammonium Thiocynate in different solvents" *J. Chem. Eng. Data., **54,** 1063-64, (2009).*

[38] J. Alvarez, R. Biltonen; "Nucleic acid-solvent interactions: temperature dependence of the heat of solution of thymine in water and ethanol." *Biopoly., **12(8)**, 1815-28, (1973).*

[39] C. Randall R. Zand R; "Microcalorimetric studies of the heats of solution of bovine myelin basic protein." *Biochim. Biophy. Acta, **831(2)**, 242-8, (1985).*

[40] E. Yonemochi, Y. Yoshihashi, K. Terada; "Quantitative relationship between solubility, initial dissolution rate and heat of solution of chiral drugs." *Pharma. Res.,**17(1)**, 90-93, (2000).*

[41] J. N. Spencer, E. S. Holmboe, M. R. Kirshenbaum, S. W. Barton, K. A. Smith, W. S. Wolbach, J. F. Powell and C. Chorazy; "Solvation of heterocyclic nitrogen compounds by methanol and water." *Can. J. Chem.*, ***60***, 1183-86 (1982).

[42] W. Huckel, J. Joachim, E. Simmersbach; "The physical properties of pyrazole, imidazole and 4-methylimidazole and of their solutions, especially in benzene." *Physik. Chem.*, ***A186***, 129-79 (1940).

[43] G. R. Berezina, Y. G. Vorob'ev, R. P. Smirnov; "Solubility of some macroheterocycles of symmetric structure in alcohols." *Z. Fiz. Khim.*, ***70***, 94-96 (1996).

[44] S. Baluja, R. Bhalodiya., M. Bhatt., N. Vekariya, R. Gajera; "Solubility of Enrofloxacin Sodium in Various Solvents at Various Temperatures" *J. Chem. Eng. Data, **53,** 2897–99, (2008).*

[45] S. Baluja, R. Bhalodiya., M. Bhatt., N. Vekariya, R. Gajera; "Solubility of Difloxacin in Acetone, Methanol, and Ethanol from (293.15 to 313.15) K" *J. Chem. Eng. Data., **54,** 1091–93, (2009).*

[46] S. Baluja; "Physicochemical Studies of Some Schiff Bases Derived From 6-Ethylbenzene 1,3-diol" *E- J. Chem.,* ***1,*** *199-205, (2004).*

[47] J. Riddick, W. Bunger, T. Sakano; "Organic Solvents-Physical Properties and methods of purification." Fourth Ed., Techniques of Chemistry, II, A Wiley-Interscience Publication, John Wiley, New York (1986).

[48] M. Zhu; "Solubility and Density of the Disodium Salt Hemiheptahydrate of Ceftriaxone in Water + Ethanol Mixtures." *J. Chem. Eng. Data.,* ***46****, 175-76, (2001).*

[49] A. Apelblat, E. Manzurola; "Solubilities of o-acetylsalicylic, 4-aminosalic, 3,5-di nitrosalicylic, and p-toluic acid, and magnesium-DL-aspartate in water from T= (278 to 348) K." *J. Chem. Thermodyn.,* ***31****, 85-91, (1999).*

[50] J. Gao, Z. Wang, D. Xu, R. Zhang; "Solubilities of Triphenylphosphine in Ethanol, 2-Propanol, Acetone, Benzene and Toluene." *J. Chem. Eng. Data,* ***52****, 189-91, (2007).*

[51] Aragon, D. M., Ruidiaz, M. A., Vargas, E. F., Bregni, C., Chiappetta, D. A., Sosnik, A., Martinez, F. "Solubility of the antimicrobial agent Triclosan in organic solvents of different hydrogen bonding capabilities at several temperatures." *J. Chem. Eng. Data,* ***53****, 2576-80, (2008).*

[52] R. Krug, W. Hunter, R. Grieger; "Enthalpy-entropy compensation. 2. Separation of the chemical from the statistical effects." *J. Phys. Chem.,* ***80****, 2341-51, (1976).*

[53] P. Bustamante, S. Romero, A. Pena, B. Escalera, A. Reillo; "Nonlinear enthalpy-entropy compensation for the solubility of drugs in solvent mixtures: paracetamol, acetanilide and nalidixic acid in dioxane-water." *J. Pharma. Sci.,* ***87****, 1590-96, (1998).*

[54] P. Kalsi; "Organic reactions and their mechanisms," New age international (P) limited- New Delhi, 2nd edition, ***119***, (2004).

[55] A. El-Bindary, A. El-Sonbati, E. El-Mosalamy, R. Ahmed; "Potentiometric and Thermodynamic Studies of Azosulfonamide Drugs. X". *Chem. Pap.,* ***57,*** *255-58, (2003).*

INTRODUCTION

Partition coefficient (P) is logarithms of the ratio of concentrations of un-ionized compound between the mixture of two immiscible solvents at equilibrium[(1)]. Hence this coefficient is a measure of differential solubility of the compound between these two solvents.

Generally water is choosen as one of the solvents while the second is hydrophobic such as octanol[(2)]. Hence both the partition or distribution coefficient

is measure for hydrophilicity (water lovingness) or hydrophobicity (water fearingness) of a chemical substance.

The knowledge of partition coefficient is highly useful in varius fields. Diethyl ether and water is a very well-known example of using partition coefficient to purify organic compounds. Moreover it is used in both branches of Pharmacology i.e. in Pharmacokinetics the distribution coefficient has a strong influence on ADME properties (Absorption, Distribution, Metabolism, and Excretion) of the drug[3] and in Pharmacodynamics the hydrophobic effect is the major driving force for the binding of drugs to their receptor targets[4-6]. Partition coefficients are useful for in estimating distribution of drugs within the body because hydrophobic drugs with high partition coefficients are distributed to hydrophobic compartments of cells such as lipid bilayers while hydrophilic drugs (low partition coefficients) are found in blood serum like hydrophilic compartments.

Many industries which are preparing various consumer products also take into account distribution coefficient for example in the formulation of cosmetics[7,8], topical ointments[9], dyes[10-12], toxicology of hair colors[13] and many other consumer products. For agrochemicals[14-16], partition coefficient is necessory to measure hydrophobicity because hydrophobic insecticides and herbicides tend to be more active but in general hydrophobic agrochemicals have longer half lives and therefore display increased risk of adverse environmental impact. In metallurgy[17, 18], the partition coefficient is an important factor in determining how different impurities are distributed between molten and solidified metal so it is a critical parameter for purification of metals and other study of metals. For environmental study the hydrophobicity of a compound can give the information of how easily a compound might be taken up in groundwater from pollute waterways, and its toxicity to animals and aquatic life.[19] In the field of hydrogeology the octanol water partition coefficient, is used to predict and model the migration of dissolved hydrophobic organic compounds in soil and groundwater[20,21].

There are many methods to determine partition coefficient. The shake-flask method[22], is classical and most reliable method of log P determination

which consists of dissolving some of the under experimental solute in a binary mixture of octanol and water by shaking, then measuring the concentration of the solute in each solvent. One of the best method is to use a carrier free radiotracer[23,24]. In this method, a known amount of a radioactive material is added to one of the phases. The two phases are then brought into contact and mixed until equilibrium has been reached. Then the two phases are separated before the radioactivity in each phase is measured. If the structure of solute chemical is known, then the faster method of log P determination is HPLC (high-performance liquid chromatography). The log P of a solute can be determined by correlating its retention time with similar compounds with known log P values.[25] Recently, some experiments on the basis of electrochemical methods using polarized liquid interfaces have been used to examine the thermodynamics and kinetics of the transfer of charged species from one phase to another. [26,27] However, the prediction of log P can also be done by using QSPR (Quantitative Structure-Property Relationship) algorithms[28-32]. Now a days, many log P calculators[33] or predictors are commercially available. Among various methods, the most common and accurate method of measuring the distribution of the solute is by UV/VIS spectroscopy. It gives accurate results for a broad range of solutes (for both neutral and charged compounds). This method has been used by various workers [34-40] for various systems.

Haydn[41] et al. measured the partition coefficient of methyl paraben between oil/water system. Jerie et al have been estimated partition coefficient for C2H4 between air and plant tissues for the study of metabolism[42]. Etxebarria et al determined the partition coefficient of 4-methylpyridine between potassium nitrate-toluene by potentiometric titration[44]. Partition coefficient of penicillin in poly(ethylene glycol)-sodium citrate aqueous systems has also been estimated[45]. The partition coefficient of coumarin derivatives[46], organohalogens [47], monobasic weak acidic compounds[48] and toluidine blue[49] have also been studied.

In the present study, partition coefficient of cyanopyridines has been studied in n-Octanol-water system by UV spectroscopy at different pH. The partition coefficient is highly affected by pH. So, in the present study, a wide range of pH (0.84 to 8.0) is selected. For 0.84 pH, 0.1 N HCl was taken whereas

for pH 6.0, 7.4 and 8.0, phosphate buffer was used. These values of pH are selected due to their existence in human body. As HCl exists in gastric juice in stomach, 0.1 N HCl is taken. Blood has 7.4 pH, so the study is done at pH 7.4. Further, the middle and upper range of body pH is 6.0 and 8.0 respectively, so study was done at these pH also.

EXPERIMENTAL

n-Octanol was of analytical grade. The purity of solvent was checked by GC (SHIMADZU- GC 14 B) and found to be 99.8%. Distilled water was used throughout for all experiments.

Preparation of standard solution:-

10 mg sample was dissolved in n-octanol to give 100 ml solution of 100 ppm. This solution was known as standard solution. λ_{max} values were measured by using UV spectrophotometer (Shimadzu, UV-1700, Pharmaspec) from this solution. Suitable dilutions were made from this standard solution (2 μg to 20 μg) and absorbance (OD) was measured. The calibration curve of OD versus concentration of compounds was drawn.

Determination of Partition coefficient:-

A known amount of the compound under investigation was dissolved in n-octanol at a concentration not higher than 20 μg. Equal volumes of this solution and water is mixed in oven dried stoppered flask and the mixture was stirred for 24 hrs. at room temperature. After 24 hrs., the solution was transferred into 60 ml of separating funnel and allow it to stand in order to separate the aqueous and organic layers. The organic layer will be upper one while lower will be aqueous. The organic layer was then analyzed by UV spectrophotometer. Using calibration curve, the concentration of compounds in organic layer was also then evaluated.

THEORY

Partition coefficient (P) is defined as the ratio of the compounds in organic phase to that present in the aqueous phase. i.e. [50],

$$P = \frac{C_{org}}{C_{aq}} \qquad \ldots (3.5.1)$$

where C_{org} and C_{aq} are concentration of solute in organic and aqueous phases respectively.

In the present case, concentrations were determined by UV measurement so, equation (3.5.1) written as [51]:

$$P = \frac{B_E}{B_E - A_E} \qquad \ldots (3.5.2)$$

where, B_E=Absorbance before extraction and A_E=Absorbance after extraction From equation (3.5.2), log P were calculated for each set of experiment.

RESULTS AND DISCUSSION

The values of log P for the studied compounds at different pH are given in Table 3.5.1. Further, log P values at different pH and water solutions are compared for all the studied compounds and are shown in Figure 3.5.1.

It is evident from Table 3.5.1 and Fig. 3.5.1 that the value of log P varies with pH for each compound. All the studied compounds have the same moiety but different side chain. Thus, log P depends upon the side chain. Further, the position of substitution affects log P. Actually, log P value depends upon the hydrophilic and hydrophobic character of compounds. log P values have inverse relation with hydrophilisity of compounds. Thus, one can say that different side chains have different hydrophilic or hydrophobic character which affects log P.

The compounds with higher log P value are hydrophobic in nature whereas those with lower log P value are hydrophilic.

Table 3.5.1 and Figure 3.5.1 shows that in water, CP-10 is highly hydrophobic in nature among all the compounds whereas CP-7 is highly hydrophilic. Thus, when there is no substitution, hydrophobicity increases whereas presence of chloro group at para position increases the hydrophilic character. So, CP-7 will easily be absorbed in blood than CP-10. Due to this reason CP-10 easily spread in body than any other studied compounds. However, it is more likely to absorb in fatty tissues [30, 31]. Overall, the decreasing order of hydrophobicity of compounds in water is: CP-10 > CP-5 > CP-8 > CP-4 > CP- 6 > CP-2 > CP-1 > CP-9 > CP-3 > CP-7.

In 0.1N HCl-octanol system, CP-8 (containing nitro group at meta position) is highly hydrophobic whereas CP-9 (containing hydroxy group at para position) is highly hydrophilic in nature. Thus, in gastric juice also, CP-8 will not be absorbed whereas CP-9 can be easily absorbed. In this case the decreasing order of hydrophobicity of compounds is: CP-8 > CP-1 > CP-5 > CP-10 > CP-3 > CP-2 > CP-7 > CP-4 > CP-6 > CP-9.

At 6.0 pH, CP-1 with methoxy group at para position to aromatic ring is highly hydrophobic in nature. While CP-6 is more hydrophilic which contains hydroxyl group at meta position. Overall the decreasing order of hydrophobicity of compounds is: CP-1 > CP-5 > CP-8 > CP-2 > CP-3 > CP-10 > CP-7 > CP-4 > CP-9 > CP-6.

In 7.4 pH range, among all these compounds CP-7 has minimum log P values whereas maximum is observed for CP-4 which can be considered more hydrophobic in nature. The decreasing order of hydrophobicity of compounds is: CP-4 > CP-2 > CP-10 > CP-1 > CP-8 > CP-5 > CP-9 > CP-6 > CP-3 > CP-7.

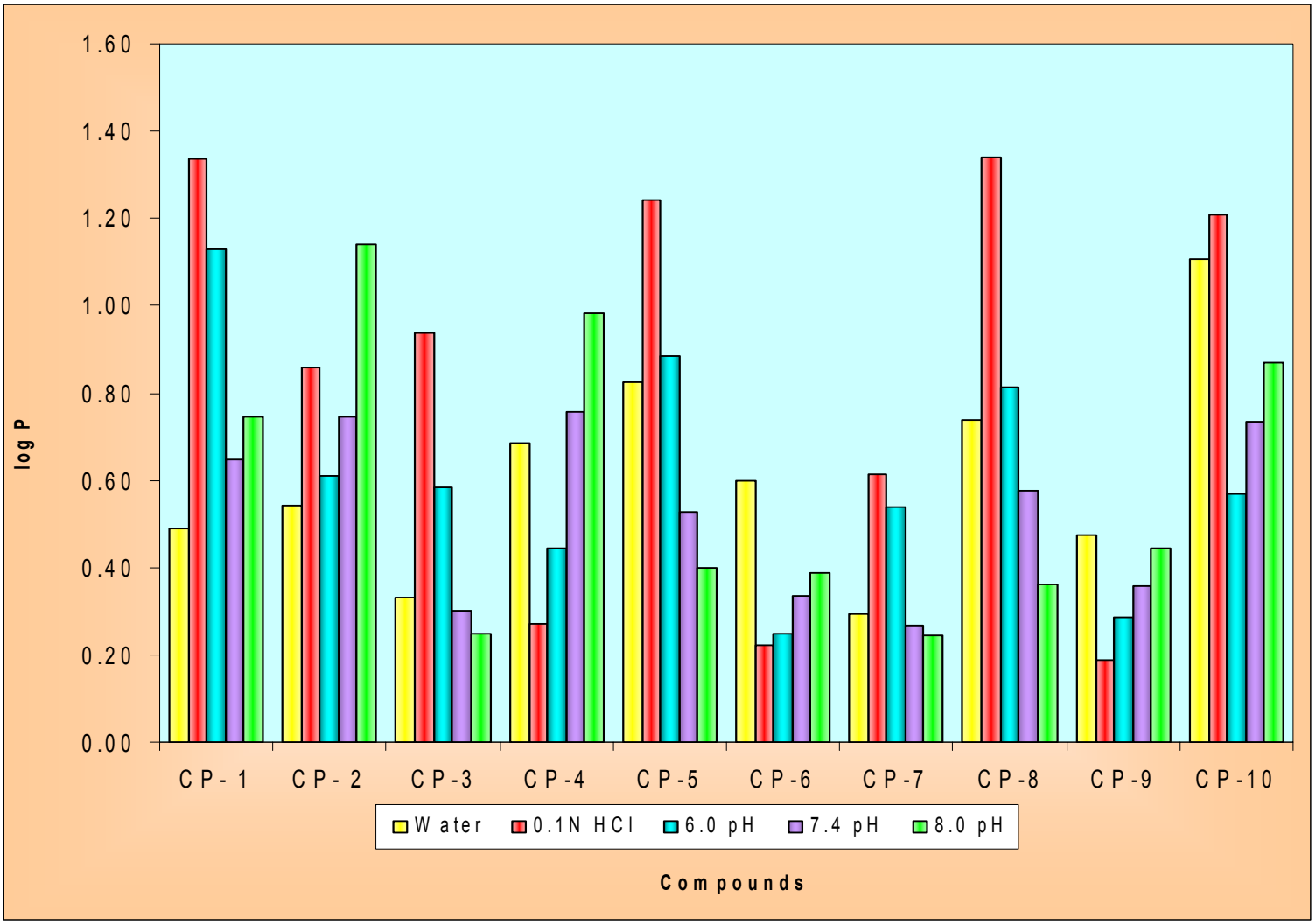
For 8 pH, CP-2 is most hydrophobic whereas CP-7 is most hydrophilic among all the studied compounds. So, due to the hydrophobic nature of CP-2 can be accumulated in lipid material [52, 53]. The decreasing order of hydrophobicity of compounds at 8 pH is: CP-2 > CP-4 > CP-10> CP-1 > CP-9 > CP-5 > CP-6 > CP-8> CP-3 > CP-7.

Over all, it is concluded that type of substitution, position of substitution and pH of solution play important role in partition coefficient.

Table 3.5.1: log P values for compounds of CP series.

Comp. code	Substituent	Max absorption Wavelength (nm)	log P				
			Water	0.1N HCl	6.0 pH	7.4 pH	8.0 pH
CP-1	4-OCH_3	325	0.4882	1.3348	1.1294	0.6491	0.7468
CP-2	4-CH_3	317	0.5432	0.8593	0.6081	0.7468	1.1392
CP-3	4-Br	312	0.3329	0.9372	0.5848	0.3013	0.2489
CP-4	4-NH_2	342	0.6861	0.2696	0.4453	0.7572	0.9814
CP-5	4-NO_2	335	0.8263	1.2434	0.8856	0.5253	0.3983
CP-6	3-OH	296	0.5970	0.2235	0.2497	0.3341	0.3881
CP-7	4-Cl	301	0.2938	0.6122	0.5402	0.2677	0.2458
CP-8	3-NO_2	332	0.7369	1.3419	0.8149	0.5746	0.3605
CP-9	4-OH	295	0.4756	0.1895	0.2850	0.3572	0.4447
CP-10	Phenyl	243	1.108	1.209	0.569	0.734	0.869

Figure 3.5.1: log P values of compounds of CP series.



REFERENCES

[1] A. Leo, C. Hansch and D. Elkins; "Partition coefficients and their uses". *Chem. Rev., **71 (6)**, 525–616, (1971).*

[2] J. Sangster; "Octanol-Water Partition Coefficients" *Funda. Phy. Chem., John Wiley Ltd., **2**,178, (1997).*

[3] H. Kubinyi; "Nonlinear dependence of biological activity on hydrophobic character: the bilinear model". *Farmaco Sci., **34 (3)**, 248–76, (1979).*

[4] D. Eisenberg, A. McLachlan; "Solvation energy in protein folding and binding". *Nature **319 (6050)**, 199–203, (1986).*

[5] S. Miyamoto and P. Kollman; "What determines the strength of noncovalent association of ligands to proteins in aqueous solution?". *Proc Natl Acad Sci USA **90 (18)**, 8402–6, (1993).*

[6] P. Vladimir, B. Testa, H. Waterbeemd; "Lipophilicity in Drug Action and Toxicology." *New York: John Wiley Ltd.. 439,(1996).*

[7] A. Bianco, E. Pramauro, M. Gallarate, M. Carlotti and G. Orio; "Determination of micelle/water partition coefficients of cosmetic preservatives. Optimization of the capillary electrophoretic method." *Anal. Chim. Acta, **412(1-2)**, 141-48, (2000).*

[8] J. Arct, A. Oborska, M. Mojski, A. Binkowska and B. Swidzikowska; "Common cosmetic hydrophilic ingredients as penetration modifiers of flavonoids." *Int. J. Cosmetic Sci., **24(6)**, 357-66 (2002).*

[9] T. Viegas, L. Winkle, P. Lehman, S. Franz and T. Franz; "Evaluation of creams and ointments as suitable formulations for peldesine." *Int. J. Pharma., **219(1-2)**, 73-80 (2001).*

[10] B. Candanedo, V. David, D. Gray; "Partitioning of charged and neutral dextran dye derivatives in biphasic cellulose nanocrystal suspensions." *Can. J. Chem., **86(6)**, 503-11 (2008).*

[11] A. Sallo, E. Seciaman, E. Sarandan, E. Crasmareanu and Z. Simon; "Lipophilicity evaluation of some monoazoic dyes and of a series of arylamides by means of partition coefficients and RP-TLC." *Annals West Uni. Timisoara, Series of Chem., **12(3)**, 1453-66 (2003).*

[12] A. Kaneko, R. Hann; "Introduction of partition coefficients to finite element dye diffusion thermal transfer model." *J. Imag. Sci. Tech., **37(5)**, 494-8 (1993).*

[13] I. Bialas, J. Arct and M. Mojski; "Safety of hair dyes use. Toxicological exposure." *J. App. Cosmeto., **27(3)**, 97-110 (2009).*

[14] E. Baker and G. Hunt; "Factors affecting foliar penetration and translocation of pesticides." *ACS Symp. Series. **371**, 8-21 (1988)*.

[15] S. Joerg and B. Peter; "Modeling penetration of plant cuticles by crop protection agents and effects of adjuvants on their rates of penetration." *Pesti. Sci., **42(3)**, 185-208 (1994).*

[16] W. Ibrahim, W. Aini, D. Hermawan, H. Mohamed, Y. Hassan; "Rapid estimation of octanol-water partition coefficient for triazole fungicides by MEKC with sodium deoxycholate as surfactant." *Chromatographia, **68(5/6)**, 415-19 (2008)*.

[17] K. Itagaki, M. Hino, R. Pagador, S. Surapunt; "Distribution of elements between liquid alloy and slag phases in extractive metallurgy." *Berichte der Bunsen-Gesellsch., **102(9)**, 1304-08 (1998).*

[18] E. Vojtech, J. Zdenek, J. Claude, J. Emil; "Zinc partitioning between glass and silicate phases in historical and modern lead-zinc metallurgical slags from the Pribram district, Czech Republic." *Comptes Rendus l'Acad. Sci., **331(4)**, 245-50 (2000)*.

[19] D. Cronin, T. Mark; "The Role of Hydrophobicity in Toxicity Prediction". *Curre. Com. Aided Drug Desi. **2 (4)**, 405–13, (2006)*.

[20] N. Simmleit, R. Herrmann; "The behavior of hydrophobic, organic micropollutants in different karst water systems. II. Filtration capacity of karst systems and pollutant sinks." *Water, Air, Soil Pollu., **34(1)**, 97-109 (1987)*.

[21] J. Arey, G. Samuel, P. Gschwend; "A physical-chemical screening model for anticipating widespread contamination of community water supply wells by gasoline constituents." *J. Contamin. Hydro., **76(1-2)**, 109-138 (2005)*.

[22] A. Hajare, M. Mali, S. Sarvagod, S. Kurane, S. Patwardhan and A. Dange" Adsorption and partition studies of Fluconzole." *Asian J. Res. Chem., **2(2)**, 213-19 (2009)*.

[23] S. Peng, W. Wang, J. Chen; "Partitioning of Trace Metals in Suspended Sediments from Huanghe and Changjiang Rivers in Eastern China." *Water, Air, Soil Poll., **148(1-4)**, 243-58 (2003)*.

[24] P. Talbot, N. Raj, E. Butelman, Y. Huang, K. Ngo" "radiotracer for imaging opioid receptors in vivo with PET: Synthesis and evaluation in baboons." *J. Nucl. Med., **46(3)**, 484-94 (2005)*.

[25] K. Valkó; "Application of high-performance liquid chromatography based measurements of lipophilicity to model biological distribution". *J. chromato., A **1037 (1-2),** 299–310, (2004)*.

[26] S. Ulmeanu, H. Jensen, G. Bouchard, P. Carrupt, H. Girault; "Water-oil partition profiling of ionized drug molecules using cyclic voltammetry and a 96-well microfilter plate system". *Pharm. Res., **20 (8)**, 1317–22, (2003)*.

[27] A. Bond, F. Marken; "Mechanistic aspects of the electron and ion transport processes across the electrode". *J. Electroanal. Chem., **372 (1-2)**, 125–35, (1994)*.

[28] A. Ghose, G. Crippen; "Atomic Physicochemical Parameters for Three-Dimensional Structure-Directed Quantitative Structure-Activity Relationships I.Partition Coefficients as a Measure of Hydrophobicity" *J. Computational Chemi., **7(4)**, 565–77, (1986)*.

[29] A. Ghose, V. Viswanadhan, J. Wendoloski; "Prediction of Hydrophobic (Lipophilic) Properties of Small Organic Molecules Using Fragmental Methods: An Analysis of AlogP and ClogP Methods". *J. Phy. Chem., A **102 (21)**, 3762–72, (1998).*

[30] H. Moriguchi, S. Hirono, Q. Liu, I. Nakagome, Y. Matsushita; "Simple method of calculating octanol/water partition coefficient". *Chem. Pharm. Bull., **40(1)**, 127-130, (1992)*.

[31] C. Hansch, A. Leo; "Substituent Constants for Correlation Analysis in Chemistry and Biology." *New York: John Wiley Ltd.,178, (1979).*

[32] A. Leo, D. Hoekman, C. Hansch; "Exploring QSAR, Hydrophobic, Electronic, and Steric Constants." *Am. Chem. Soc., (1995).*

[33] I. Tetko, G. Poda; "Property-based logP prediction" *Molec. Drug Prop. Measur. Predic., Wiley-VCH. (2007).*

[34] A. Taherpour, A. Taherpour, Z. Taherpour, O. Taherpour; "Relationship study of octanol-water partitioning coefficients and total biodegradation of linear simple conjugated polyene and carotene compounds by use of the Randic index and maximum UV wavelength." *Phy. Chem. Liq., **47(4),** 349-359 (2009).*

[35] B. Marschner, R. Winkler, D. Joedemann; "Factors controlling the partitioning of pyrene to dissolved organic matter extracted from different soils." *Eur. J. Soil Sci., **56(3)**, 299-306 (2005).*

[36] S. Kumbar, A. Kulkarni, A. Dave and T. Aminabhavi; "An assessment of solubility profiles of structurally similar hazardous pesticide in water + methanol mixture and co-solvent effect on partition coefficient." *J. Hazardous Mat., **89(2-3)**, 233-39 (2002).*

[37] V. Dohnal, D. Fenclova; "Air-Water Partitioning and Aqueous Solubility of Phenols." *J. Chem. Eng. Data, **40(2)**, 478-83 (1995).*

[38] A. Constantinescu, M. Ionescu, D. Mihailescu, D. Margineanu; "Partition coefficients of tertiary amines between aqueous solutions and unilamellar liposomes." *Rev. Roumaine Biochimie., **25(3)**, 269-74 (1988).*

[39] P. Mukerjee and J. Cardinal; "Benzene derivatives and naphthalene solubilized in micelles. Polarity of microenvironments, location and distribution in micelles, and correlation with surface activity in hydrocarbon-water systems." *J. Phy. Chem., **82(14)**, 1620-7 (1978).*

[40] H. Fung, W. Conway; "Student experiment in pharmaceutics." The pH partitioning of a weak acid." *Am. J. Pharma. Edu., **38(4)**, 523-30 (1974).*

[41] B. Haydn, G. Konning, J. Thomas, "Significance of the partition coefficient of a preservative in cosmetic emulsions." *Am. Perf. Cosmetics, **85(3)**, 61-5 (1970).*

[42] P. Jerie, A. Shaari, M. Zeroni and M. Hall; "The partition coefficient of ethylene-14C in plant tissue as a screening test for metabolism or compartmentation of ethylene." *New Phytologist, **81(3)**, 499-504 (1978).*

[43] A. Meulemans, P. Vicart, J. Mohler, D. Henzel, M. Vulpillat; "Permeability of nitroimidazoles in rat cortex." Chemotherapy, ***32(6)***, 486-93 (1986).

[44] N. Etxebarria, M. Zapatero, J. Castresana, L. Fernandez, M. Olazabal, J. Madariaga; "Determination of the protonation constant and partition coefficient of 4-

methylpyridine in potassium nitrate - toluene at 25˚ C." *J. Sol. Chem., **20(12)**, 1213-25 (1991).*

[45] J. Marcos, L. Fonseca, M. Ramalho, J. Cabral; "Variation of penicillin acylase partition coefficient with phase volume ratio in poly(ethylene glycol)-sodium citrate aqueous two-phase systems." J. chromatography." *Biomed. Sci. appl., **711(1-2)**, 295-9 (1998).*

[46] B. Jayshree, A. Sahu, M. Murthy, K. Venugopala; "Synthesis, determination of partition coefficient and antimicrobial activity of triazolothiadiazinylbromocoumarin derivatives." *Mat. Sci. Res. Ind., **3(2)**, 187-190 (2005)*.

[47] S. Gao, C. Cao; "A new approach on estimation of solubility and n-octanol/water partition coefficient for organohalogen compounds." Int. J. Mol. Sci., 9(6), 962-77 (2008).

[48] X. Ming, S. Han, V. Shu, C. Zheng, D. Sheng, H. zhen; "Chromatographic retention prediction and octanol-water partition coefficient determination of monobasic weak acidic compounds in ion-suppression reversed-phase liquid chromatography using acids as ion-suppressors." *Talanta, **79(3)**, 752-61(2009)*.

[49] J. Liu, A. Zou, B. Mu; "Toluidine blue: Aggregation properties and distribution behavior in surfactin micelle solution." *Collo. Surfaces, Bioint., **75(2)**, 496-500 (2010)*.

[50] H. Sawyer, Beebe; "Chemistry Experiments for Instrumental Analysis" *Wiley (1984)*

[51] B. Jayshree, A. Sahu, M. Murthy and K. Venugopala; "Synthesis, determination of partition coefficient and antimicrobial activity of triazole thiadiazinyl bromocoumarin derivatives" *Mat. Sci. Res. Ind., **3(2)**, 187-90 (2005).*

[52] E. Rowe, F. Zhang, T. Leung, J. Parr and P. Guy; "Thermodynamics of Membrane Partitioning for a Series of n-Alcohols Determined by Titration Calorimetry: Role of Hydrophobic Effects." *Biochemistry, **37(8)**, 2430-40 (1998).*

[53] M. Fresta, S. Guccione, A. R. Beccari, P. M. Furneri and G. Puglisi; "Combining molecular modeling with experimental methodologies: mechanism of membrane permeation and accumulation of ofloxacin." *Bioorg. Med. Chem., **10(12)**, 3871-89 (2002).*

INTRODUCTION

During the past few years, the methods of thermal analysis have been widely accepted in various branches of science to study thermal properties of pharmaceuticals, polymers, clays, minerals, metals alloys etc. Studies on thermal properties of substances are of great importance from both scientific as well as practical point of view. The study of thermal properties provide information about various material properties e.g. melting process, polymorphic transformations, temperature of initiation, establish thermal stability, crystallinity, stability of crystallites, glass transition temperature, cross-linking and heat of polymerization, curing behavior, influence of corrosion, oxidation or reduction as well as magnetic transitions, denaturizing behavior, vapor pressure, analytical criteria such as identification and purity [1-9] etc.

These thermal properties can be studied by various thermal techniques which are among the most powerful experimental tools developed during the last century. In these techniques, the changes in the properties of material are followed as a function of temperature when it is heated or cooled at constant predetermined rate under specified ambient atmospheric conditions.

Some of the most commonly used techniques are Differential Scanning Calorimetry (DSC), Differential Thermal Analysis (DTA), Thermo Gravimetric Analysis (TGA), Evolved Gas Detection (EGD), Evolved Gas Analysis (EGA) etc. In the present study, thermal analysis is done by DSC and TGA techniques.

DSC is a versatile thermal technique used to provide quantitative and qualitative information about physical and chemical changes involving endothermic or exothermic processes or heat capacity changes.

In TGA, the mass of sample is recorded as a function of temperature or time, when it is subjected to a programmed temperature change in a specified atmosphere. The plot of mass change versus temperature is known as thermogram or TG curve. These thermograms are characteristic for a given compound because of unique sequence of physicochemical reactions which occur over definite temperature ranges and at rates that are a function of molecular structure. The variation in weight is due to various physical and

chemical changes which lead to the evolution of volatile products or the formation of heavier reaction products [10].

So, thermal analysis is important not only for the basic characterization of materials but also in various fields such as medical science[11-13], biology[14-20], biochemistry[21-23], chemistry[24-29], soil and earth science[30-32], forensic science[33-36], marine science[37-40], electronics[41-43], nanotechnology[44-46], agriculture[47-54], space science[55-57], environment science[58-60], metallurgy and materials science[61-63], archaeology[64-66], solid waste management[67-69] etc. The knowledge of thermal properties of technical components in chemical reactors is often a key characteristic for planning and designing chemical engineering processes and process engineering[70].

Thermal analysis is also widely useful for the study of reaction kinetics[71] , investigation of gas -solid reactions[72], ligands, salts and metal complexes[73, 74], study of non-stoichiometric metal oxides[75], comparative quality assessment of coke[76], quality control of solidification processes[77], study of polymorph and different crystal forms[78, 79], drug-polymer interactions and for pre-formulation studies of pharmaceutical dosage forms[80], thermal stability of energetic explosive materials[81, 82] etc.

Thermal techniques are used in research laboratories of various industries like pharmaceutical[83-89], food[90-94], oil and fat[95-97] , flavor, perfume and cosmetic[98, 99], dye[100-101], paper and textile[102-103], petrochemical[104-107], glass[108-111], ceramic[112, 113], cement[114-116], paints and adhesives[118, 120] etc.

Literature survey shows that thermal analysis of various types of compounds such as drugs[120], polymers[121-124], nuclear and other conventional fuel[125-127], ionic liquid[128-129], liquid crystals[130, 131], inorganic[132-134] and organic[135-138] compounds have been reported.

In the present study, thermal properties of some new synthesized cyanopyridines have been studied by DSC and TGA techniques. Using thermograms, thermal stability and various kinetic parameters have been evaluated.

THEORY

From TGA curves, various kinetic parameters can be evaluated by several methods. In all these methods, it is assumed that thermal and diffusion barriers are negligible because small quantity of material is used. The shape of any TGA curve depends on the nature of apparatus and the way in which it is used. Further, Arrhenius equation is valid in all these methods.

The kinetic treatments are generally based on the relationship of the type:

$$dC/dt = K f(C) \quad \text{... (3.6.1)}$$

where C is the degree of conversion, t is time and K is rate constant. $f(C)$ is a temperature independent function of C.

The constant K is assumed to have the Arrhenius form:

$$K = A e^{-E/RT} \quad \text{... (3.6.2)}$$

C can also be defined as:

$$C = 1-(W/W_0) \quad \text{... (3.6.3)}$$

where W_0 and W are the initial weight at $t=0$ and weight at any time t of the material.

Equation (3.6.3) can be written as:

$$(W/W_0) = (1-C) \quad \text{... (3.6.4)}$$

W/W_0 is known as residual weight fraction.

Thus, the rate of conversion is,

$$dC/dt = -(1/W_0)(dW/dt) \quad \text{... (3.6.5)}$$

For homogeneous kinetics, the conversion is assumed to be of the form:

$$f(C) = (1-C)^n \quad \text{... (3.6.6)}$$

where n is the order of the reaction.

Substituting the values from equation (3.6.2) and (3.6.6) in equation (3.6.1) gives:

$$dC/dt = A\, e^{-E/RT} (1-C)^n$$

or $$dC/dt = (A/\beta)\, e^{-E/RT} (1-C)^n \quad \text{... (3.6.7)}$$

where A is the frequency factor, β is the rate of heating and E is the energy of activation.

Various methods for single and multiple heating rates have been reported. The methods of single heating rate are as follows:

1. Freeman-Carroll [139] and Anderson-Freeman Method [140]:

At a single heating rate, Freeman and Carroll gave the following relation to analysis TGA data:

$$\ln (dC/dt)/\ln (1-C) = n - E/R\, [(1/T)/(\Delta \ln(1-C)] \quad \text{... (3.6.8)}$$

A plot of left hand side against $(1/T)/(\Delta \ln(1-C))$ gives a straight line with a slope equal to $-E/R$ and the intercept is equal to n.

Anderson and Freeman then derived the following equation by using equation (3.6.8):

$$(\Delta \ln[dC/dt]) = n\, (\Delta \ln(1-C)) - E/R\, \Delta(1/T) \quad \text{... (3.6.9)}$$

The plot of $(\Delta \ln[dC/dt])$ against $(\Delta \ln(1-C))$ for equal intervals of $\Delta(1/T)$ gives a straight line with slope equal to n and intercept $-E/R\Delta(1/T)$.

2. Sharp-Wentworth method [141]:

To analyse the TGA data for first order kinetics (n=1), Sharp and Wentworth gave the relation:

$$\log [(dC/dt)/(1-C)] = \log (A/\beta) - (E/2.303R).(1/T) \quad \text{... (3.6.10)}$$

The plot of $\log [(dC/dt)/(1-C)]$ against $1/T$ would be a straight line with slope equal to $-(E/2.303R)$ and intercept equal to $\log (A/\beta)$.

3. Chatterjee Method [142]:

Based on the weight units, the following relation was developed by Chatterjee:

$$n = [\log(dW/dt)_1 - \log(dW/dt)_2] / (\log W_1 - \log W_2) \quad \text{... (3.6.11)}$$

where W_1 and W_2 are the sample weights.

4. Horowitz and Metzger method [143]:

In this method, the value of energy of activation E can be determined from a single TG curve by the relation:

$$ln\,[ln(1-C)^{-1}] = (E/RT_s^2)\theta \quad \text{... (3.6.12)}$$

where $\theta = T-T_s$. T_s is the temperature at which the rate of decomposition is maximum. The frequency factor A and entropy change ΔS can be determined by the following equations:

$$ln\,E - ln\,(RT_s^2) = ln\,A - ln\beta - E/RT_s \quad \text{... (3.6.13)}$$

$$A = (k_bT / h)\, e^{\Delta S/R} \quad \text{... (3.6.14)}$$

where k_b is Boltzmann constant and h is Planck's constant.

EXPERIMENTAL

Thermo gravimetric analysis (TGA) and Differential Scanning Calorimetry (DSC) measurements were made on the instrument "Pyris-1, Perkin Elmer Thermal Analysis" at the heating rate of 10°C/min in nitrogen atmosphere for all the cyanopyridine derivatives.

RESULTS AND DISCUSSION

The TGA thermograms of CP-1 and CP-2 are given in Figure 3.6.1. Various thermal properties such as initial decomposition temperature (IDT), the decomposition temperature range and the maximum degradation along with the percentage weight loss are reported in Table 3.6.1.

For some compounds, degradation is single step process whereas for others, it is multistep process. For CP-1, CP-4 and CP-9, multi step degradation takes place.

Table 3.6.1 shows that CP-7 is most unstable whereas CP-9 is very stable followed by CP-1, CP-3, CP-4 and CP-6. All the studied compounds have a common moiety with different constituents as side chain. Thus, the stability of the compounds depends upon the substituent group. When hydroxyl group is present at para position (as in CP-9), stability is highest which is followed by the presence of hydroxyl group at meta position (as in CP -6). The presence of other groups such as p-methoxy (in CP-1), p-bromo (in CP-3) and p-amino (in CP-4) also shows increases the stability.

Further, various kinetic parameters, such as order of the degradation (n), energy of activation (E), frequency factor (A) and entropy change (ΔS^o) have also been calculated from the thermograms for each step and are reported in Table 3.6.2.

It is evident from Tables 3.6.2 that order of reaction is quite different in different steps for different cyanopyridines. For single step degradation compound, order of reaction varies from 0.38 to 10.68, whereas for multi steps it varies from 0.25 to 6.4.

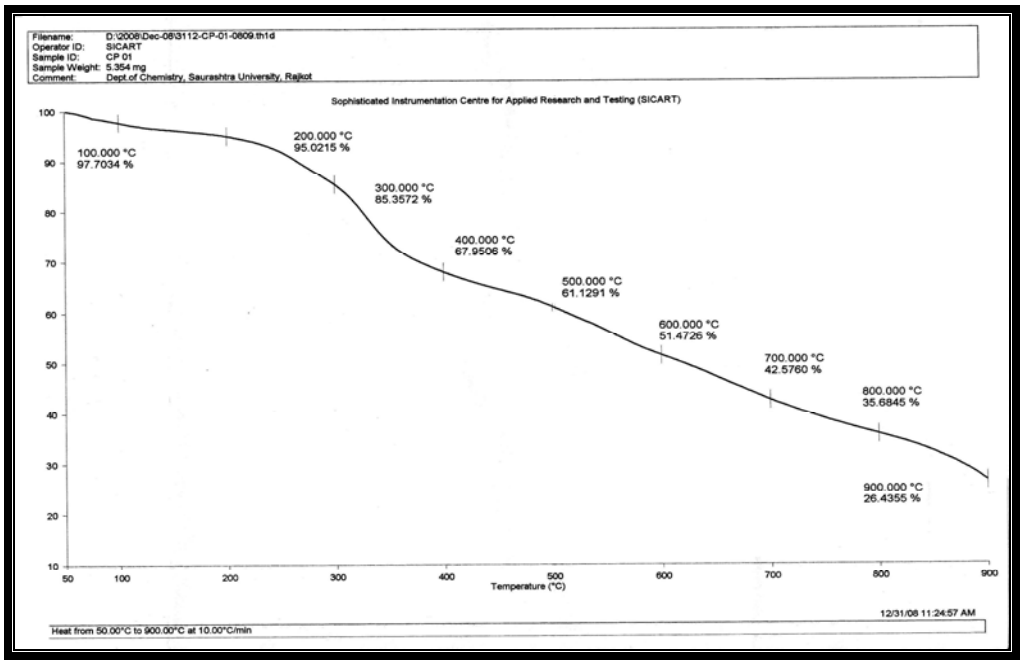
For single step degradation compounds, energy of activation (E) is maximum for CP-2 and minimum for CP-8. The frequency factor (A) also varies in the same order. For multi step degradation compounds, in first and second steps, energy of activation is found to be maximum for CP-9 in second step and minimum for the second step of CP-4. The frequency factor A follows the same order.

Further, change in entropy (ΔS^0) for all these reactions were calculated by equation (3.6.14) and are reported in Table 3.6.2. These values are both positive and negative for different compounds. The positive values of ΔS^0

indicate that the transition state is less ordered than the original compound whereas negative value of ΔS^0 corresponds to an increase in the order of transition state than the reactants.

Further, DSC of these compounds was also studied. Figure 3.6.2 shows the DSC of CP-6 and CP-7. The melting points determined from DSC are reported in Table 3.6.1 along with the melting temperature determined by open capillary method. It is observed that the melting temperatures determined by the two methods are in good agreement for most of the cases.

Figure 3.6.1: The TGA graphs of CP-1 and CP-2.



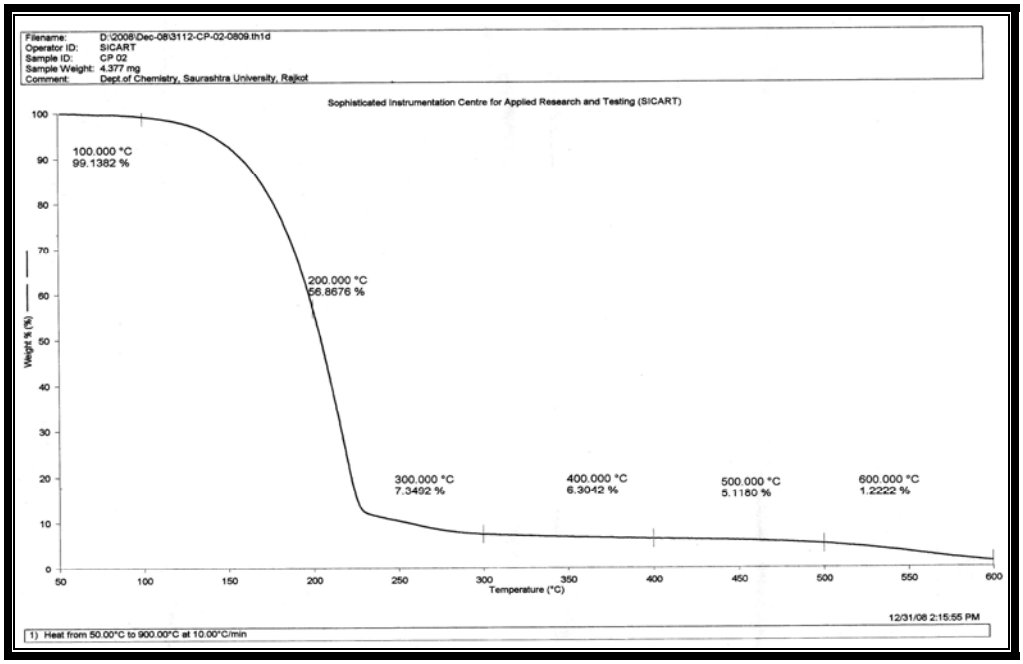
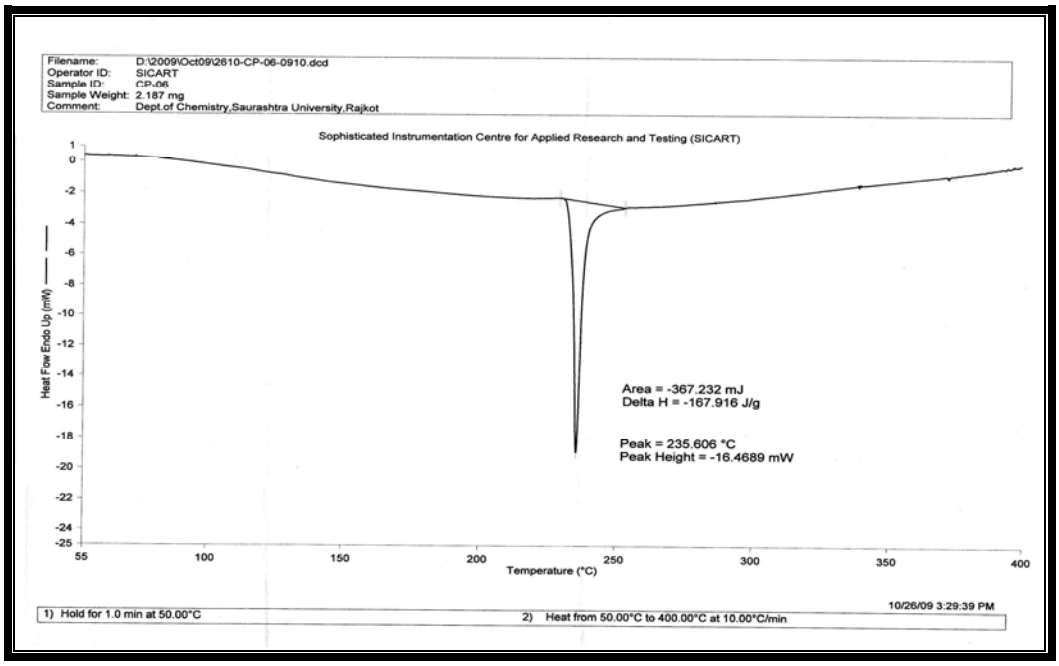


Figure 3.6.2: The DSC graphs of CP-6 and CP-7.



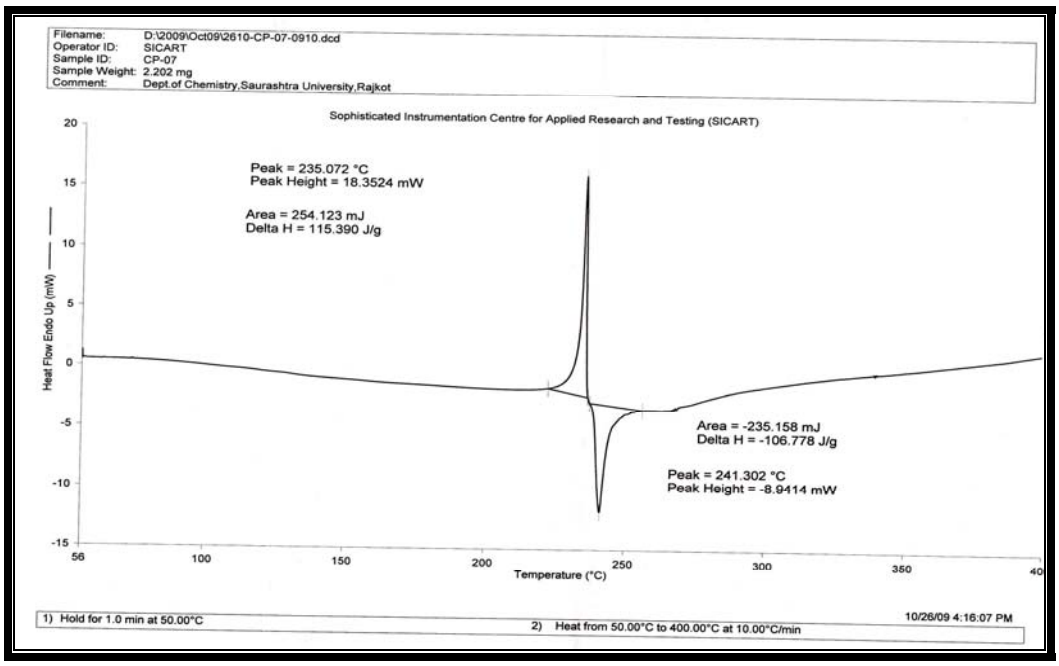


Table 3.6.1: TGA/DSC data for synthesized CP series.

Comp. Code	*Amt. mg.*	*Initial Decomp. Temp. ^oC*	*Decomp. range ^oC*	*% Wt. loss*	*Residual Wt. Loss mg.*	*DSC ^0C*	*Open capillary method ^0C*
CP-1	5.354	200	200-700	57.424	3.074	228	221
CP -2	4.377	150	150-300	92.65	4.026	178	180
CP -3	5.636	200	200-700	42.90	2.417	214	214
CP -4	5.469	200	200-705	46.80	2.559	202	208
CP -5	5.028	173	150-897	42.57	2.140	182	187
CP -6	3.648	200	200-700	52.14	1.902	235	235
CP -7	5.951	100	100-599	47.80	2.844	235	234
CP -8	4.017	185	185-800	47.88	1.923	206	201
CP -9	5.941	205	205-750	40.57	2.410	229	229
CP -10	4.364	150	150-600	35.74	1.559	158	162

Table 3.6.2: The kinetic parameters of cyanopyridine derivatives.

Comp. code	*n*	*E* *kJ.mol^{-1}*	*A* *s^{-1}*	*ΔS* *J.mol^{-1}.K^{-1}*
CP-1 1st step	2.25	67.49	1.68 X 10^{10}	103.13
CP-1 2nd step	1.39	65.63	3.02 X 10^{03}	-32.68
CP -2	0.38	276.63	1.02 X 10^{17}	225.43
CP -3	1.90	128.35	1.14 X 10^{25}	349.86
CP -4 1st step	0.25	56.701	6.25 X 10^{09}	96.01
CP -4 2nd step	1.17	45.73	8.74 X 10^{01}	-48.91
CP -4 3rd step	2.50	241.86	7.81 X 10^{12}	60.49
CP -5	1.79	153.49	1.11 X 10^{17}	230.93
CP -6	6.60	205.42	1.39 X 10^{37}	619.54
CP -7	7.88	97.49	2.39 X 10^{17}	241.16
CP -8	10.68	17.33	1.14 X 10^{02}	-52.43
CP -9 1st step	2.30	73.09	3.47 X 10^{11}	128.57
CP -9 2nd step	6.40	854.21	2.68 X 10^{84}	1519.72
CP -10	5.10	107.33	1.69 X 10^{22}	335.19

REFERENCES

[1] E. H. Asswad, J. Dewaele, J. Nagy, R. Hubert, Z. Gabelica, E. Derouane, F. Crea, R. Aiello, A. and Nastro; "Identification of different tetrapropylammonium cations occluded in ZSM-5 zeolite by combined thermal analysis (TG-DTA) and carbon-13 NMR spectroscopy." *Zeolites,* ***8(3),*** *221-7 (1988).*

[2] R. Bedard, C. Bowes, N. Coombs, A. Holmes, T. Jiang, S. Kirkby, P. Macdonald, A. Malek and G. Ozin; "Cloverite: exploring the 30-.ANG. supercage for advanced materials science applications." *J. Am. Chem. Soc.,* ***115(6),*** *2300-13 (1993).*

[3] J. Zhou and M. Lamvik; "Heat transfer in the solidification and melting processes of metallic materials and its application to the determination of thermal conduction." *Heat Trans. Sci. Tech., 1996, [Int. Sym. Heat Trans.], 4th, Beijing, 113-18 (1996).*

[4] D. Webster, S. David and J. Cao; "A novel technique for characterizing polymeric materials - proton magnetic resonance thermal analysis." *Cur. Trends in Poly. Sci.,* ***1,*** *147-155 (1996).*

[5] N. Kutaish, P. Aggarwal and D. Dollimore; "Thermal analysis of calcium oxalate samples obtained by various preparative routes." *Thermochim. Acta,* ***297(1-2),*** *131-37 (1997).*

[6] T. Lada, K. Przybylski, A. Morawski, J. Prazuch and T. Brylewski; "Application of high-pressure DTA for high-pressure liquid-phase epitaxy of doped mercury and thallium HTS formations." *J. Therm. Anal. Calor.,* ***66(2),*** *611-15 (2001).*

[7] A. Molena, V. Camila, C. Luci, L. Marcio, V. Marcus and A. Guastaldi; "Comparison of crystallinity between natural hydroxyapatite and synthetic cp-Ti/HA coatings." *Mat. Res., (2005),* ***8(2),*** *207-11.*

[8] N. Mohalik, D. Panigrahi and V. Singh; "Application of thermal analysis techniques to assess proneness of coal to spontaneous heating." *J. Thermal Anal. Calori.,* ***98(2),*** *507-19 (2009).*

[9] G. Sacha and S. Nail; "Thermal analysis of frozen solutions: Multiple glass transitions in amorphous systems." *J. Pharma. Sci.,* ***98(9),*** *3397-05 (2009).*

[10] H. H. Willard, L. L. Merritt, Jr. J. A. Dean, F. A. settle, Jr., "*Instrumental Methods of Analysis" Sixth Edition (1986).*

[11] M. Jaffe; "The importance of thermal analysis in biorelevant characterization of polymeric biomaterials." *Proc. NATAS Ann. Con. Thermal Ana. App., 33rd 126. 50. 259/1-2 (2005).*

[12] G. Balint, P. Than, I. Doman, N. Wiegand, G. Horvath and D. Lorinczy; "Calorimetric examination of the human meniscus." *J. Thermal Anal. Calori.,* ***95(3),*** *759-61 (2009).*

[13] M. Abuladze, V. Sokhadze, E. Namchevadze, E. Kiziria, L. Tabatadze and L. Lejava; "Thermal analysis of whole bacterial cells exposed to potassium permanganate using differential scanning calorimetry: a biphasic dose-dependent response to stress." *Sci. World J.,* ***9,*** *109-17 (2009).*

[14] B. Mitchell and A. Birnie; "Biological materials [studied by DTA]." *Differ. Therm. Anal., **1,** 673-04 (1970).*

[15] E. Dubler and B. Kamber; "Thermal analysis of biogenic solid compounds." *Therm. Anal., [Proc. Int. Conf. Therm. Anal.], **6,** 531-9 (1980).*

[16] J. Lelievre; "Thermal analysis of carbohydrates as illustrated by aqueous starch systems." *Carbohydr. Chem., 137-61 (1992).*

[17] D. Milardi, C. Rosa, D. Grasso; "Theoretical basis for differential scanning calorimetric analysis of multimeric proteins." *Biophy. Chem., **62(1-3),** 95-108 (1996).*

[18] H. Hinz, F. Schwarz; "Measurement and analysis of results obtained on biological substances with d.s.c." *J. Chem. Thermodyn., **33(11),** 1511-25 (2001).*

[19] A. Thanonkaew, S. Benjakul and W. Visessanguan; "Chemical composition and thermal property of cuttlefish (Sepia pharaonis) muscle." *J. Food Comp. Anal., **19(2-3),** 127-33 (2005).*

[20] J. Bourgeois, L. Pierson, J. Nicolas, M. Lalanne, P. Couvreur and K. Andrieux; "Application of thermal analysis to the study of lipidic prodrug incorporation into nanocarriers." *J. Thermal Anal. Calori., **98(1),** 65-71 (2009).*

[21] L. Collett and M. Brown; "Biochemical and biological applications of thermal analysis." *J. Thermal Anal. Calori., **51(2),** 693-26 (1998).*

[22] G. Santiago, B. Delgado, A. Blanca and J. Mas-Oliva; "Thermal analysis of the plasma membrane Ca2+-ATPase." *Mole. Cellular Biochem., **209(1&2),** 105-12 (2000).*

[23] Y. Kosheleva and S. Trofimov; "Characteristics of the Biochemical Composition of Plant Litter at Different Stages of Decomposition *Bio. Bull., **35(1),** 64-69 (2008).*

[24] Z. Roshchina and N. Selivanova; "Thermal stability of potassium hydrogen selenites." *Trudy Ins. – Mos. Khim. Tekh. Ins., **67,** 8-9 (1970).*

[25] A. Rahman; "Application of thermal analysis in surface chemical investigation of zirconia gels." *Thermochim. Acta., **85**, 3-13 (1985).*

[26] H. Cammenga and M. Epple; "Basic principles of thermoanalytical techniques and their applications in preparative chemistry." *Angewandte Chemie, **34(11),** 1171-87 (1995).*

[27] H. Tanaka and N. Koga; "Thermal analysis and kinetics of solid-state reactions: its applications to education in chemistry." *J. Thermal Anal. Calori., **56(2),** 855-61 (1999).*

[28] Chowdhury, B; "The role of thermal analysis in chemistry and material science." *Monograph Series Int. Con. Coord. Chem. , **5,** 43-50 (2001).*

[29] S. Baluja, K. Vaishnani and N. Kachhadia; "Thermal study of some Schiff bases of p-aminophenol." *J. Ultra Sci. Phy. Sci., **21(1),** 67-72 (2009).*

[30] Y. Marumo, S. Nagatsuka and Y. Oba; "Clay mineralogical analysis using the <0.05-mm fraction for forensic science investigation - its application to volcanic ash soils and yellow-brown forest soils." *J. Forensic Sci., **31(1),** 92-05 (1986).*

[31] W. Eysel; "Thermal analysis in Earth sciences." *Thermochim. Acta;* ***110,*** *495-9 (1987).*

[32] A. Plante, J. Fernandez and J. Leifeld; "Application of thermal analysis techniques in soil science." *Geoderma,* ***153(1-2),*** *1-10 (2009).*

[33] R. Curini, S. Zamponi, F. D'Ascenzo, C. De Angelis, A. Marino and A. Dezzi; "Thermal analytical techniques applied to the narcotic field: cocaine analysis." *Thermochim. Acta;* ***153,*** *11-26 (1989).*

[34] R. Alan; "Thermal analysis as an aid to forensics : alkane melting and oxidative stability of wool." *Thermochim. Acta,* ***324(1-2),*** *151-62 (1998).*

[35] T. Schaefer; "Analytical chemistry in forensic technology. Murders, arson, and explosive attacks." *Chemie in Unserer Zeit,* ***38(6),*** *392-98 (2004).*

[36] R. Medeiros, F. Antoniosi Filho, R. Nelson and G. Leles; "Development of forensic analytical chemistry method for examination of Merla by thermal analysis and high resolution gas chromatography." *J. Thermal Anal. Calori.,* ***97(1),*** *337-42 (2009).*

[37] B. Fry, E. Peltzer, C. Hopkinson, A. Nolin, L. Redmond; "Analysis of marine DOC using a dry combustion method." *Marine Chem.,* ***54(3/4)****, 191-01 (1996).*

[38] L. Pane, E. Franceschi, L. De Nuccio and A. Carli; "Applications of thermal analysis on the marine phytoplankton, Tetraselmis suecica." *J. Thermal Anal. Calori.,* ***66(1),*** *145-54 (2001).*

[39] M. Giovanela, E. Parlanti, S. Soriano, M. Soldi, M. Sierra, "Elemental compositions, FT-IR spectra and thermal behavior of sedimentary fulvic and humic acids from aquatic and terrestrial environments." *Geochem. J.,* ***38(3),*** *255-64 (2004).*

[40] M. Rodriguez-Barroso, S. Ramirez-del, E. Blanco, J. Quiroga and M. Garcia; "Qualitative Estimation of Heavy Metals in Marine Sediment Using Thermal Analysis." *Soil Sediment Conta.,* ***17(2),*** *107-20 (2008).*

[41] M. Judd and M. Pope; "Formation and surface properties of electron emissive coatings. VII. Commercial cathode coatings." *A. Therm; Proc. Int. Conf., 3rd,* ***2,*** *777-92 (1972).*

[42] P. Gallagher; "Thermoanalytical characterization of electronic materials." *Thermochim. Acta,* ***88(1),*** *85-100 (1985).*

[43] T. Ozawa, T. Kaneko and T. Sunose; "Historical review on research of kinetics in thermal analysis and thermal endurance of electrical insulating materials. II. Thermal endurance evaluation by thermal analysis." *J. Thermal Anal.,* ***47(4),*** *1105-20 (1996).*

[44] Y. Xiao, L. Liu, W. Chin, T. Lin, K. Mya, J. Huang and X. Lu; " Nano-hybrid luminescent dot: synthesis, characterization and optical properties." *J. Mat. Chem.,* ***16(9),*** *829-36 (2006).*

[45] N. Rajalakshmi, N. Lakshmi, K. Dhathathreyan; "Nano titanium oxide catalyst support for proton exchange membrane fuel cells." *Int. J. Hydro. Eng.,* ***33(24),*** *7521-26 (2008).*

[46] S. Hooker, R. Geiss, R, R. Schilt and A. Kar; "Rapid inspection of carbon nanotube quality." *Cera. Eng. Sci. Proc., **28(6),** 119-30 (2008).*

[47] W. Brennan; "Applications of thermal analysis in the food, dairy and agricultural industries. A review." *Thermal Anal. App. Study., **16,** 13 (1976).*

[48] S. Hook; "Dye-binding capacity as a sensitive index for the thermal denaturation of wheat protein. A test for heat-damaged wheat." *J. Sci. Food Agri., **31(1),** 67-81 (1980).*

[49] P. Mader, V. Haber, J. Zelinka; "Classical dry ashing of biological and agricultural materials. Part I. Following the course of removal of organic matrix." *Analusis, **25(6),** 175-83 (1997).*

[50] T. Lupascu, I. Dranca, V. Popa and M. Vass; "Application of thermal analysis to the study of some waste agricultural products for the preparation of active carbons." *J. Thermal Anal. Calori., **63(3),** 855-63 (2001).*

[51] S. Arvelakis, H. Gehrmann, M. Beckmann, E. Koukios; "Studying the ash behavior of agricultural residues using thermal analysis." *J. Thermal Anal. Calori., **72(3),** 1019-30 (2003).*

[52] S. Munir, S. Daood, W. Nimmo, A. Cunliffe and B. Gibbs; "Thermal analysis and devolatilization kinetics of cotton stalk, sugar cane bagasse and shea meal under nitrogen and air atmospheres." *Biores. Tech., **100(3),** 1413-18 (2008).*

[53] C. Vasile and M. Popescu; "Thermal behaviour/treatment of some vegetable residues. II. Spanish broom (Spartium junceum) fibers." *Cellulose Chem. Tech., **42(7-8),** 335-44 (2008).*

[54] S. Arora, M. Kumar, G. Dubey; "Thermal decomposition kinetics of rice husk: activation energy with dynamic thermogravimetric analysis." *J. Energy Ins., **82(3),** 138-43 (2009).*

[55] G. Bayer and H. Wiedemann, "Simultaneous thermal and x-ray analysis of lunar samples and of minerals." *Natur wissenschaften, **60(6),** 299-300 (1973).*

[56] G. Gorbunov, R. Medvedev and V. Chashnikov; "Preliminary results of the determinations of physical properties of lunar rock microfragments from the Luna-16 and Luna-20 samples." *Doklady Akademii Nauk., **283(3),** 601-4 (1985).*

[57] A. Buch, R. Sternberg, C. Szopa, C. Freissinet, C. Garnier, E. Bekri, C. Rodier, G. Navarro, F. Raulin, M. Cabane, M. Stambouli, D. Glavin and P. Mahaffy; "Development of a gas chromatography compatible sample processing (SPS) for the in-situ analysis of refractory organic matter in martian soil: preliminary results." *Adv. Space Res., **43(1),** 143-51 (2009).*

[58] A. Kettrup and G. Matuschek; "The role of thermal analysis in environmental protection." *J. Thermal Anal., **47(2),** 317-30 (1996).*

[59] D. Price; "Thermal analysis in industrial environments." *J. Thermal Anal., **49(2),** 953-59 (1997).*

[60] M. Rahman and L. Chambers; "Analysis of volatile organic compounds in air by thermal desorption." *LCGC North America,* ***21,*** *(2009).*

[61] F. Sale, A. Taylor; "Applications in metallurgy and materials science." *Royal Soc. Chem.,* ***117,*** *197-21 (1992).*

[62] P. Hack, W. Xie, B. Sisk and W. Pan; "Micro-thermal analysis and its applications in material science." *Proc. NATAS Ann. Conf. Thermal Anal. Appl.,* ***29,*** *580-85 (2001).*

[63] B. Chowdhury; "The role of thermal analysis in chemistry and material science." Monograph Series, Int. Conf. Coordi. Chem., ***5,*** *43-50 (2001).*

[64] J. Pires and A. Cruz, "Techniques of thermal analysis applied to the study of cultural heritage." *J. Thermal Anal. Calori.,* ***87(2),*** *411-15 (2007).*

[65] A. Krapukaityte, S. Tautkus and A. Kareiva; "Thermal analysis - A powerful tool for the characterization of pottery." *Chemija,* ***19(2),*** *4-8 (2008).*

[66] G. Lombardi and M. Santarelli; "Multi-instrumental analysis of asphalts of archaeological interest." *J. Thermal Anal. Calori.,* ***96(2),*** *541-46 (2009).*

[67] T. Lupascu, I. Dranca, V. Popa and M. Vass; "Application of thermal analysis to the study of some waste agricultural products for the preparation of active carbons." *J. Thermal Anal. Calori.,* ***63(3),*** *855-63 (2001).*

[68] M. Som, L. Lemee and A. Ambles; "Stability and maturity of a green waste and biowaste compost assessed on the basis of a molecular study using spectroscopy, thermal analysis , thermodesorption and thermochemolysis." *Bioresource Tech.,* ***100(19),*** *4404-16 (2009).*

[69] J. Zheng, Y. Jin, Y. Chi, J. Wen, X. Jiang; "Pyrolysis characteristics of organic components of municipal solid waste at high heating rates." *Waste Manag.,,* ***29(3),*** *1089-1094 (2009).*

[70] Y. Mei; M. Liu, S. Wu, J. Chi and C. Shu; "Thermal explosion and runaway reaction simulation of lauroyl peroxide by DSC tests." *J. Thermal Anal. Calori.,* ***96(3),*** *777-82 (2009).*

[71] H. Zhang, F. Zhao, J. Yi, X. Zhang, Z. Rong and Y. Su; "Preparation, thermal behavior and nonisothermal decomposition reaction kinetics of cerium 3,5-dinitrosalicylate(CeDNS)." *Wuji Huaxue Xuebao* ***25(5),*** *869-874 (2009).*

[72] K. Jaenicke-Roessler, G. Leitner and F. Mueller; "Investigation of gas -solid reactions by means of thermal analysis /mass spectrometry." *Fresenius' J. Anal. Chem.,* ***349(1-3),*** *170-1 (1994).*

[73] E. Antina, G. Gusev, E. Rumyantsev and N. Dudina; "Thermal properties of ligands, salts and metal complexes of linear oligopyrroles." *Rus. J. Gen. Chem.,* ***79(9),*** *1900 - 09 (2009).*

[74] J. Sanders, P. Gallagher; "Kinetic analysis of complex decomposition reactions using evolved gas analysis." *J. Thermal Anal. Calori.,* ***96(3),*** *805-11 (2009).*

[75] S. Jasienska and J. Orewczyk; "Thermal analyses in the investigation of non-stoichiometric metal oxides." *Thermochim., Acta.,* ***93,*** *477-80 (1985).*

[76] T. Mukherjee, H. Ray; "Thermal analysis of blast furnace coke for comparative quality assessment." *Steel India,* ***28(1)****, 9-13 (2005).*

[77] D. Emadi, L. Whiting, S. Nafisi, R. Ghomashchi; "Applications of thermal analysis in quality control of solidification processes." *J. Thermal Anal. Calori.,* ***81(1),*** *235-42 (2005).*

[78] J. Baronsky, S. Bongaerts, M. Traeubel, H. Weiss Hans-Christoph, N. Urbanetz; "The study of different solid forms of Emodepside." *Eur. J. Pharma. Biopharma., official j. Arbeits. Pharma. Verfahre.,* ***71(1),*** *88-99 (2009).*

[79] M. Barrio, P. Espeau, J. Tamarit, M. Perrin, N. Veglio Nestor; R. Ceolin; "Polymorphism of progesterone: relative stabilities of the orthorhombic phases I and II inferred from topological and experimental pressure-temperature phase diagrams." *J. Pharma. Sci.,* ***98(5),*** *1657-70 (2009).*

[80] A. Antonio, R. Matos, J. Formariz, T. Pedroni, R. Gustavo, S. Maria, T. Egito, E. Socrates, G. Oliveira; "Thermal behavior and stability of biodegradable spray - dried microparticles containing triamcinolone." *Int. J. Pharma.,* ***368(1-2),*** *45-55 (2009).*

[81] L.. Collins and L. Haws; "The thermochemistry of explosives: a review." *Thermochim. Acta,* ***21(1),*** *1-38 (1977).*

[82] M. Hemmila; "Use of thermal analysis in compatibility testing of 2,4,6-trinitrotoluene." *J. Thermal Anal.,* ***25(1),*** *135-8 (1982).*

[83] A. Radecki, M. Wesolowski; "Analysis of some pharmaceutical preparations by thermal decomposition." *Acta Pharma. Jugoslavica,* ***28(3-4),*** *155-9 (1978).*

[84] F. Khattab; "Thermal analysis of pharmaceutical compounds." *Thermochim. Acta,* ***61(3),*** *253-68 (1983).*

[85] M. Hardy; "Pharmaceutical applications of thermal analysis." *Royal Soc. Chem.,* ***117,*** *180-97 (1992).*

[86] A. Barnes, M. Hardy, T. Lever; "A review of the applications of thermal methods within the pharmaceutical industry." *J. Thermal Anal.,* ***40(2),*** *499-509 (1993).*

[87] R. Bottom; "Thermal analysis: Solving problems in the pharmaceutical industry." *Pharma. Tech. Eur.,* ***13(11),*** *40-2 (2001).*

[88] D. Giron "Applications of Thermal Analysis and Coupled Techniques in Pharmaceutical Industry" *J. Thermal Anal. Calori.,* ***68(2),*** *335-57 (2002).*

[89] M. Klous, G. Bronner, B. Nuijen, R. van, M. Jan, J. Beijnen; "Pharmaceutical heroin for inhalation: Thermal analysis and recovery experiments after volatilisation." *J. Pharma. Biomed. Anal.,* ***39(5),*** *944-50 (2005).*

[90] B. Van, A. Martinus; "Heat-induced deamidation, dephosphorylation and breakdown of caseinate." *Int. Dairy J.,* ***9(3/6),*** *237-241, (1999),*

[91] P. Aggarwal, D. Dollimore; "Degradation of starchy food material by thermal analysis." *Thermochimica Acta, 57-63 (2000).*

[92] C. Mothe, G. Cheila, M. Mothe, E. Bach; "Evaluation of mushrooms, Agaricus, by thermal analysis." Proc. NATAS Ann. Conf. Thermal Anal. Appl., 33rd 055.20.051/1-4 (2005) .

[93] S. Vecchio, L. Cerretani, A. Bendini, E. Chiavaro; "Thermal Decomposition Study of Monovarietal Extra pure Olive Oil by Simultaneous Thermogravimetry/Differential Scanning Calorimetry: Relation with Chemical Composition." *J. Agri. Food Chem., **57(11),** 4793-4800 (2009).*

[94] A. Sandoval, M. Nunez, A. Mueller, G. Valle and D. Lourdin; "Glass transition temperatures of a ready to eat breakfast cereal formulation and its main components determined by DSC and DMTA." *Carbohy. Poly., **76(4),** 528-534 (2009).*

[95] C. Tan, Y. Man; "Differential scanning calorimetric analysis of edible oils: comparison of thermal properties and chemical composition." *J. Am. Oil Chem. Soc., **77(2),** 143-155 (2000).*

[96] G. Galchenko, M. Vyhrestyuk, O. Chygyrynets and G. Stovpchenko, "Study of the chemical composition of wastes of the oil and fat industry." *Ekotekhnologii i Resursosberezhenie, **(5),** 55-57, (2005)*

[97] T. Streibel, A. Fendt, R. Geissler, E. Kaisersberger, T. Denner and R. Zimmermann; "Thermal analysis/mass spectrometry using soft photo-ionisation for the investigation of biomass and mineral oils." *J. Thermal Anal. Calori., **97(2),** 615-19 (2009).*

[98] P. Phang, D. Dollimore; "The analysis of perfume fixatives by simultaneous TG-DTA studies and rising temperature kinetics." *Proc. Conf. Am. Thermal Anal. Soc., **26**, 13-15, 508-13 (1998).*

[99] F. Feng, H. Weibing, L. Hongxia, Y. Ainong, H. Tingneng; "Synthesis and thermal analysis of a flavor of 2,2-bibenzyl-1,3,5-trithiane." *Shipin Keji, **(4),** 130-32 (2008).*

[100] C. Oliveira, M. Ana, M. Oliveira, L. Rodrigues, M. Silva and M. Smith; "Thermal analysis of a polymorphic azo dye derived from 2-amino-5-nitrothiazole." *Thermochim. Acta., **453(1),** 52-56 (2007).*

[101] A. Rotaru, G. Bratulescu and P. Rotaru; "Thermal analysis of azoic dyes: Part I. Non-isothermal decomposition kinetics of [4-(4-chlorobenzyloxy)-3-methylphenyl](p-tolyl)diazene in dynamic air atmosphere." *Thermochim. Acta., **489(1-2),** 63-69 (2009).*

[102] F. Beall; "Differential calorimetric analysis of wood and wood components." *Wood Sci. and Tech., **5(3),** 159-75 (1971).*

[103] E. Karmazsin; "Thermal analysis in the cellulose, paper and textile industry." *Thermochim. Acta, **110,** 471-5 (1987).*

[104] R. Konyashina and T. Nikiforova; "Chemical composition of thermal cracking kerosine. " *Tr. Inst. Goryuch. Iskop. Min. Ugol. Prom. SSSR, **25(1),** 153-7 (1970).*

[105] H. Faust; "The thermal analysis of waxes and petrolatums." *Thermochim. Acta ., **26(1-3),** 383-98 (1978).*

[106] N. Saikia, P. Sengupta, P. Gogoi and P. Borthakur; "Thermogravimetric combustion kinetics of petroleum effluent treatment plant sludge." *J. Thermal Anal. Calori.,* ***79(3),*** *653-62 (2005).*

[107] A. Weitz and B. Wunderlich; "Thermal analysis and dilatometry of glasses formed under elevated pressure." *J. Poly. Sci. Poly. Phy.,* ***12(12),*** *2473-91 (1974).*

[108] R. Speyer and S. Risbud; "Methods for the determination of the activation energy of glass crystallization from thermal analysis." *Phy. Chem. Glasses* ***24(1),*** *26-30 (1983).*

[109] N. otov, C. Wagner, F. Bellido, L. Rodriguez, G. Jimenez-Garay; "Thermal analysis of Ag-As-Se chalcogenide glasses." *Thermochim., Acta,* ***296(1-2),*** *23-9 (1997).*

[110] H. Thomas, V. Thomas, R. Ramanujan, M. Anantharaman; "Thermal and structural analysis of the crystallization dynamics of metallic glass - Fe40Ni38B18Mo4." *J. Optoelec. Adv. Mat.,* ***11(8),*** *1094-99 (2009).*

[111] J. Fischer, V. Kraemer, M. Salk and J. Strub; "Thermal analyses of the dental glass-ceramic Dicor in regard to the development of a two-layered texture." Thermochim. Acta, ***160(1),*** 39-42 (1990)

[112] U. Shayachmetov, I. Dranca; "Use of methods of thermal analysis in studying ceramic materials on the basis of Al2O3, ZrO2, Si3N4, SiC and inorganic binder." J. Thermal Ana. Calorimetry , ***64(3),*** 1153-61 (2001).

[113] B. Dietrich, G. Schell, E. Bucharsky, R. Oberacker, M. Hoffmann, W. Schabel, M. Kind, H. Martin; "Determination of the thermal properties of ceramic sponges." *Int. J. Heat Mass Trans.,* ***53(1-3),*** *198-05 (2010).*

[114] S. Handoo, S. Raina; "Cement raw mix characterization by differential thermal analysis." *Thermochim., Acta,* ***93,*** *609-12 (1985).*

[115] S. Mojumdar, M. Drabik, A. Ray; "Macro-defect-free (MDF) cements: thermal analysis , moisture resistance, chemical, SEM and magnetic analyses." *Proc. NATAS Ann. Conf. Thermal Anal. Appl.,* ***30,*** *545-50 (2002).*

[116] I. Vidican, B. Phan, J. Farr, N. Norton,; "XRF, XRD, and thermal analysis techniques for quantitative determination of Portland cement and slag cement constituents." *J. ASTM Int.,* ***5(9),*** *(2008).*

[117] V. Chincholkar and V. Kamble; "DTA of some random paint samples." *J. Ind. Aca. Foren. Sci.,* ***24(2),*** *12-21 (1985).*

[118] C. McGlinchey; "Thermal analysis of fresh and mature oil paint films: the effect of pigments as driers and the solvent leaching of mature paint films." *Mat. Res. Soc. Symp. Proc.,* ***185(2),*** *93-103 (1991).*

[119] Z. Czech, R. Pelech; "Thermal decomposition of polyurethane pressure-sensitive adhesives dispersions." *Prog. Org. Coatings,* ***67(1),*** *72-75 (2010).*

[120] D. Bikiaris, G. Papageorgiou, A. Stergiou, E. Pavlidou, E. Karavas, F. Kanaze, M. Georgarakis; "Physicochemical studies on solid dispersions of poorly water-soluble drugs: Evaluation of capabilities and limitations of thermal analysis techniques." Thermochim. Acta, ***439(1-2),*** 58-67 (2005).

[121] G. Marosi, P. Anna, G. Bertalan, A. Tohl, R. Lagner, I. Balogh, I. Papp; "Thermal analysis of fiber forming polymers. Multiphase systems." *J. Thermal Ana., **47(2),** 463-73 (1996).*

[122] J. Kaloustian, J. Pastor; "Chemical and thermal analysis of the biopolymers in the lavandin." *J. App. Poly. Sci., **77(7),** 1629-41 (2000).*

[123] A. Leszczynska, K. Pielichowski; "Application of thermal analysis methods for characterization of polymer/montmorillonite nanocomposites." *J. Thermal Anal. Calorimetry, **93(3),** 677-87 (2008).*

[124] K. Karger; "Thermal Analysis of Polymers: Fundamentals and Applications by J. D. Menczel and R. B. Prime." *Macromole. Chem. Phy., **210(19),** 1661 (2009).*

[125] A. Haykiri, S. Kucukbayrak and G. Okten; "Thermal analysis of different fossil fuels." *Fuel Sci. Tech. Int., **11(11),** 1611-27 (1993).*

[126] C. Lopez, D. Ammerman, A. Suo and K. Ahti; "Thermal analysis of spent nuclear fuel packages exposed to selected severe historic accidents involving fires." *Annu. Meeting Proc. Inst. Nuc. Mat. Manag., **46,** 156.240/1-8 (2005).*

[127] M. Husnawan, H. Masjuki, T. Mahlia and M. Saifullah; "Thermal analysis of cylinder head carbon deposits from single cylinder diesel engine fueled by palm oil-diesel fuel emulsions." *App. Eneg., **86(10),** 2107-13 (2009).*

[128] D. Fox, J. Gilman, A. Morgan, J. Shields, P. Maupin, R. Lyon, L. De Long and P. Trulove; "Flammability and Thermal Analysis Characterization of Imidazolium-Based Ionic Liquids." *Ind. Eng. Chem. Res., **47(16),** 6327-32 (2008).*

[129] A. Chagnes, H. Allouchi, B. Carre and D. Lemordant; "Thermal analysis of butyrolactone + 1 butyl-3-methyl-imidazolium ionic liquids mixtures." *Solid State Ionics, 176(15-16), 1419-27 (2005).*

[130] D. Obadovic, A. Vajda, M. Garic, A. Bubnov, V. Hamplova and M. Kaspar; "Thermal analysis and X-ray studies of chiral ferroelectric liquid crystalline materials and their binary mixtures." *J. Thermal Anal. Calori., **82(2),** 519-23 (2005).*

[131] C. Zhuang, X. Tang, D. Wang, A. Xia, W. Lian and Y. Shi; "An unsymmetrical porphyrin and its metal complexes: synthesis, spectroscopy, thermal analysis and liquid crystal properties." *J. Serb. Chem. Soc., **74(10),** 1097-04 (2009).*

[132] C. Earnest, W. Brennan and R. Fyans; "Characterization of the low temperature ash component of coals using multiple atmosphere DTA, TG, and DTG techniques." *Therm. Anal., Proc. ICTA, **8,** 361-4 (1985).*

[133] K. Ciuffi, H. Sacco, J. Valim, C. Manso, O. Serra, O. Nascimento, E. Vidoto and Y. Iamamoto, "Polymeric organic-inorganic hybrid material containing iron(III) porphyrin using sol-gel process." *J. Non-Crystalline Solids, **247,** 146-52 (1999).*

[134] E. M. Brown and P. K. Gallagher; "Handbook of thermal analysis and calorimetry, volume 2, applications to inorganic and miscellaneous materials." *J. Thermal Anal. Calori., **82(1),** 291-92 (2005).*

[135] A. Colak, F. Colak, D. Akduman, O. Yesilel and O. Bueyuekguengoer; "Syntheses, crystal structures, spectral and thermal analysis and biological activities of copper(II)-pyridine-2,5-dicarboxylate complexes with 4-methylimidazole, imidazole, and 3,4-dimethylpyridine." *Solid State Sci.,* ***11(11),*** *1908-18 (2009).*

[136] T. Wadsten; "Some practical findings for TA (thermal analysis) in organic and pharmaceutical industry." *J. Thermal Anal.,* ***47(2),*** *525-33 (1996).*

[137] T. Guerfel, M. Bdiri and A. Jouini; "Structure, thermal behavior, and IR investigation of a new organic sulfate." *J. Chem. Crystallo.,* ***29(11),*** *1205-10 (1999).*

[138] E. Charsley, P. Laye, V. Palakollu, J. Rooney and B. Joseph; "DSC studies on organic melting point temperature standards." *Thermochim. Acta;* ***446(1-2),*** *29-32 (2006).*

[139] E. S. Freeman, B. Carroll; The application of thermoanalytical techniques to reaction kinetics. The thermogravimetric evaluation of the kinetics of the decomposition of calcium oxalate monohydrate, *J. Phys. Chem*., **62**, *394-97 (1958).*

[140] D. A. Anderson, E. S. Freeman; Kinetics of the thermal degradation of polystyrene and polyethylene, *J. Polym. Sci*., **54**, *253-60 (1961).*

[141] J. H. Sharp, S. A. Wentworth; Kinetic analysis of thermogravimetric data, *Anal. Chem*., **41**, *2060-62 (1969).*

[142] P. K. Chatterjee; Application of thermogravimetric techniques to reaction kinetics, *J. Polym. Sci*., **3**, *4253-62 (1965).*

[143] H. H. Horowitz, G. Metzger; New analysis of thermogravimetric traces, *Anal. Chem*., **35**, *1464-68 (1963).*

INTRODUCTION

Acid dissociation constants are important parameters to indicate the extent of ionization of molecules in solution at different pH values.

The dissociation or ionization constant is determined by determining one of the species, at equilibrium. The activity or concentration of the others can be calculated from the amount of the acid or base initially introduced and the stoichiometry of the acid base equilibrium.

Literature survey shows that various methods have been used to determine the dissociation constant. Hansen and Hafliger have determined the dissociation constant of a weak acid using a dissolution rate method[1]. Kovach et al. have studied the dissociation constants of organic electrolytes using the Fuoss-Kraus method[2]. The separation methods (HPLC and CE) have also been used for the determination of dissociation constants[3]. Various workers have determined the dissociation constant by capillary electrophoresis[4], NMR methods[5], feedback-based flow ratiometry[6], spectrophotometric[7], interfacial Fourier transform infrared spectroscopy[8] , potentiometry including pH metry[9], conductometry, solubility measurements [10], cryoscopy[11], measurements of the rates of acid catalyzed hydrolysis of esters[12], measurement of the relative distribution of an acid between two immiscible solvents[13] and magnetic measurements.

Spectrophotometer method is considered to be an ideal method when a substance is not soluble enough for potentiometry or when its pK_a value is particularly low or high[14-17]. (less than 2 or more than 11). The method depends on the direct determination of the molecular species, that is the neutral molecules to the corresponding ionized species in a series of nonabsorbing buffer solutions where pH values are either known or measured. It is applicable if at least one of the species at equilibrium absorbs characteristically in the ultraviolet or visible region and the relevant ionic species show absorption maxima at different wavelengths. Various workers have used spectro photometric technique for the determination of dissociation constant[18-21].

There are many applications of dissociation constants. The nature of the functional groups can be determined by simple comparison of acidity or

dissociation constant of the unknown compound with those of known compounds. The dissociation or formation constant also provide useful informations about tautomeric equilibria [22,23], solvent-solute interactions[24] etc. The acidity constants of organic reagents play a fundamental role in many analytical procedures such as acid- base titration, solvent extraction, complex formation and ion transport. It has been shown that the acid- base properties affect the toxicity[25], chromatographic retention behavior and pharmaceutical properties[26] of organic acids and bases. Much of the theoretical foundation of modern organic chemistry is based on the observation of the effects on acid-base equilibrium of changing molecular structure[27].

Literature survey shows that the dissociation constant of various types of substances have been measured. Few workers have studied dissociation constant of complex substances[28-32]. Sandra et al have determined dissociation constants of active pharmaceutical ingredients[33]. The dissociation constants of 1,2,4-triazole and tetrazole compounds have been evaluated by comparing solvation models[34]. Alexander has determined dissociation of polyvalent electrolytes[35]. The acid-base behavior of some substituted azo dyes[36] and tetracyclines[37] were also studied. Reardon et al. have reported the dissociation constants for alkali earth and sodium borate ion pairs[38]. Shukla et al. have studied proton dissociation constants of benzoylacetone and isonitrosobenzoylacetone in aqueous-dioxane media[39]. The second dissociation constants of some amino acids were also determined using potentiometric measurement[40]. Evagelou et al. have reported the dissociation constants of the cephalosporins, cefepime and cefpirome by using UV spectrometry and pH potentiometry. By measuring dissociation constant of some compounds, thermodynamic parameters have been evaluated[41,43].

In the present work, the dissociation constant of all synthesized cyanopyridines (CP series) have been studied in dimethyl formamide by spectrophotometric technique.

EXPERIMENTAL

The synthesized cyanopyridines were recrystallized from DMF. DMF used in the present study was of LR grade and was distilled by the reported method [44].

100 ppm solution of sample was prepared in DMF. This solution known as standard solution was used to determine λ_{max} using UV spectrophotometer (SHIMADZU PHARMA SPEC-1700 UV VISIBLE) equipped with 1 cm path length cell, controlled by computer. The instrument was calibrated by usual procedure.

The following set of mixtures were prepared for determination of pK_a values

2 ml HNO_3 (0.01 M) + 4 ml $NaNO_3$ (0.01 M) + 19 ml DMF

2 ml HNO_3 (0.01 M) + 4 ml $NaNO_3$ (0.01 M) + 2 ml ligand solution (15 ppm) + 17 ml DMF

Thus, total volume of each set of solution was 25 ml and DMF:water ratio was 90:10(v/v).

To each set of solution, pH and absorbance (OD) were measured after each addition of 0.1 ml NaOH till there was no change in absorbance.

A systronic pH meter (Model No. EQ 664) was used for the pH determination. pH meter was calibrated by known buffer solutions. The glass electrode and a saturated calomel electrode were used as indicator and reference electrodes respectively.

THEORY

The protonation of a weak B can be represented as:

$$BH^+ \rightleftharpoons B + H^+ \quad \text{..... (3.7.1)}$$

So, the equilibrium constant (K) can be given as:

$$K = \frac{a_{H^+}.a_B}{a_{BH^+}} \quad \text{..... (3.7.2)}$$

where (a) represents the activity of each species. The activity (a) is related to concentration (c) by the equation:

$$a = c.\gamma \quad \text{..... (3.7.3)}$$

where γ is the activity coefficient.

Substituting the values of (a) in eq. (3.7.2) gives,

$$K = a_{H^+}.\frac{\gamma_B}{\gamma_{BH^+}}\frac{[B]}{[BH^+]} \quad \text{..... (3.7.4)}$$

where square brackets indicate the concentration of the species.

Combining the activity coefficient with K yields the mixed conditional constant K_a (one that incorporates both activity and concentration) [45] gives:

$$K_a = a_{H^+}.\frac{[B]}{[BH^+]} \quad \text{..... (3.7.5)}$$

Taking logarithm of above equation (3.7.5) gives:

$$pK_a = pH + \log\frac{[BH^+]}{[B]} \quad \text{..... (3.7.6)}$$

Rearrangement of above equation gives:

$$\log\frac{[B]}{[BH^+]} = pH - pK_a \quad \text{..... (3.7.7)}$$

A plot of $\log\frac{[B]}{[BH^+]}$ versus pH will therefore yield a straight line and pH=pK_a when $\log\frac{[B]}{[BH^+]}$ =0, providing that the temperature and ionic strength are held constant [45].

Concentrations of the individual species BH^+ and B can be determined by UV spectrophotometer by measuring the absorbance (OD) at particular wavelength. However, if a series of solutions is prepared at various pH and the total concentration of compound c_t = $[BH^+]$+[B] is constant, it can be shown that the ratio of the conjugate forms is given by[46]

$$\frac{C_a}{C_b} = \frac{A - A_b^0}{A_a^0 - A} = I \qquad (A_a^0 > A_b^0) \qquad \text{..... (3.7.8 a)}$$

or

$$\frac{C_a}{C_b} = \frac{A_b^0 - A}{A - A_a^0} = I \qquad (A_b^0 > A_a^0) \qquad \text{..... (3.7.8 b)}$$

where C_a and C_b represent $[BH^+]$ and [B] respectively, and A_a^0 and A_b^0 represent the absorbance when $[BH^+]=c_t$ and $[B] = c_t$ respectively. A plot of absorbance, obtained on the series of solutions at a single wavelength, can then plotted according to equation (3.7.7) to determine pK_a.

However, for some weak bases, it is reported that if slope 'm' of the plot (Fig-3.7.2) is not unity. In that case, pK_a value should be calculated by the following equation[47]:

$$pK_a = m.H^{1/2} \qquad \text{..... (3.7.9)}$$

where $H^{1/2}$ represents the pH at half protonation at log I=0.

RESULTS AND DISCUSSION

Table 3.7.1 shows the experimental data of pH and absorbance (OD) for the studied compounds. The plot of absorbance versus pH is shown in Figure 3.7.1 for CP-01. Using equation 3.7.8 (a or b), log I value were calculated and were plotted against pH. The plot is a straight line. In the studied compounds, the slope (m) of the plots was also calculated and the values vary between 0.86 and 0.93. It is reported [48, 49] that if m values are between 0.85 and 1.05 then the bases are of Hammett type. In that case, slope can be taken as unity. Thus, in the present study, compounds are of Hammett type and so $H^{1/2}$ is equal to pK_a. The $H^{1/2}$ values for all compounds are reported in Table 3.7.2 along with their correlation coefficients.

Further, at each pH, from the absorbance data, pK_a value was evaluated from equation (3.7.7) and average of this is reported in Table 3.7.2 along with the value calculated from the graph. It is observed that the pK_a values evaluated from the graph are in good agreement with those calculated from equation (3.7.7).

Table 3.7.3 shows the increasing order of acidity or basicity of compounds. It is observed that the NH_2 groups at para position of the phenyl ring makes CP-04 the least acidic or most basic one as expected, whereas CP-07 is found to be most acidic due to the chloro group at para position.

Table 3.7.1. Experimental data of pH and Absorbance (OD) of Cyanopyridines.

CP-01 (λ_{max} = 325)		CP -02 (λ_{max} = 317)		CP -03 (λ_{max} = 312)		CP -04 (λ_{max} = 342)		CP -05 (λ_{max} = 335)	
pH	**OD**	**pH**	**OD**	**pH**	**OD**	**pH**	**OD**	**pH**	**OD**
2.75	1.5107	2.81	1.5006	2.59	1.4825	2.57	1.5119	3.02	1.5022
3.76	1.5095	3.53	1.4988	2.98	1.4801	3.48	1.5093	3.92	1.4988
4.49	1.5064	4.61	1.4943	3.51	1.4772	4.45	1.5033	5.07	1.4915
5.63	1.4993	5.3	1.4895	4.04	1.4718	5.67	1.4978	5.88	1.4862
6.31	1.4842	6.78	1.4755	4.83	1.4636	6.33	1.4891	7.21	1.4625
7.37	1.4728	7.89	1.4423	5.56	1.4436	7.27	1.4771	7.42	1.4556
7.84	1.4523	8.31	1.4066	6.17	1.4362	7.92	1.453	7.96	1.4104
8.76	1.3998	8.57	1.3615	6.87	1.4202	8.51	1.3914	8.68	1.3199
9.41	1.2248	9.26	1.2836	7.26	1.4034	9.87	1.2246	9.53	1.2358
10.65	1.1821	10.11	1.1989	7.95	1.3526	10.49	1.1799	10.33	1.1671
11.17	1.1559	11.05	1.16	8.6	1.2845	11.25	1.1578	11.31	1.1532
11.73	1.1392	11.78	1.1432	9.5	1.1952	11.5	1.1458	11.65	1.1498
12.46	1.1352	12.34	1.1371	10.06	1.1651	12.38	1.1352	12.21	1.1406
12.89	1.1336	12.55	1.1359	11.28	1.1468	12.65	1.1322	12.61	1.1388
13.4	1.1318	13.02	1.1335	12.31	1.1314	13.02	1.1299	12.98	1.1331

Continue……

……Continue

CP -06 (λ_{max} = 296)		CP -07 (λ_{max} = 301)		CP -08 (λ_{max} = 332)		CP -09 (λ_{max} = 295)		CP -10 (λ_{max} = 243)	
pH	**OD**	**pH**	**OD**	**pH**	**OD**	**pH**	**OD**	**pH**	**OD**
3.09	1.5006	2.89	1.4817	2.7	1.4992	2.21	1.4911	2.61	1.5107
3.94	1.4985	3.22	1.4792	3.4	1.498	3.05	1.4884	3.39	1.5095
4.51	1.4963	4.36	1.477	4.16	1.4958	4.33	1.4802	4.31	1.5064
5.78	1.4855	5.68	1.4652	5.28	1.4897	5.61	1.4692	5.49	1.4993
6.88	1.4611	6.42	1.4531	6.32	1.4821	6.55	1.4564	6.51	1.4842
7.53	1.4124	7.27	1.4187	7.49	1.4428	7.37	1.4187	7.06	1.4728
8.01	1.3625	7.93	1.3604	7.99	1.4031	7.89	1.3653	7.76	1.4523
8.43	1.3222	8.37	1.2888	8.39	1.3602	8.53	1.3036	8.31	1.3998
9.21	1.246	9.25	1.2077	9.41	1.2751	9.14	1.2271	9.64	1.2248
10.26	1.1725	10.21	1.1556	10.12	1.2122	10.19	1.1641	10.57	1.1821
11.38	1.1413	11.33	1.1416	11.28	1.1536	11.22	1.1399	11.06	1.1559
11.88	1.1381	11.96	1.1331	11.66	1.1478	11.98	1.1374	12.46	1.1392
12.57	1.136	12.35	1.1304	12.47	1.1381	12.12	1.1349	12.65	1.1352
12.72	1.1356	12.67	1.1298	12.86	1.1358	12.85	1.1331	12.8	1.1336
12.92	1.1351	12.91	1.1273	13.03	1.1324	12.96	1.1317	12.93	1.1318

Table 3.7.2 : pK_a value from graph and average pK_a of cyanopyridines.

Compounds	pK_a value from graph ($H^{1/2}$)	Average pK_a value	Correlation coefficient
CP-1	8.64	8.63	0.9964
CP-2	8.99	8.65	0.9792
CP-3	8.40	7.34	0.9854
CP-4	9.10	8.65	0.9723
CP-5	8.79	8.73	0.9876
CP-6	8.57	8.44	0.9902
CP-7	8.32	8.41	0.9925
CP-8	8.80	8.65	0.9953
CP-9	8.45	8.32	0.9846
CP-10	8.81	8.66	0.9886

Table 3.7.3 Arrange cyanopyridines in order of increasing acidity or decreasing basicity strength by half protonation values as follows:

Compound Code	**$H^{1/2}$**	**Groups**	**Acidity or basicity**
CP-04	9.10	4-NH_2	**Decreasing basicity or increasing acidity** ↓ / ↑ **increasing basicity or Decreasing acidity**
CP-02	8.99	-CH_3	
CP-10	8.81	-phenyl	
CP-08	8.80	3-NO_2	
CP-05	8.78	4-NO_2	
CP-01	8.64	4-OCH_3	
CP-06	8.57	3-OH	
CP-09	8.45	4-OH	
CP-03	8.40	4-Br	
CP-07	8.32	4-Cl	

Figure 3.7.1: The variation of absorbance (OD) with pH for CP-01.

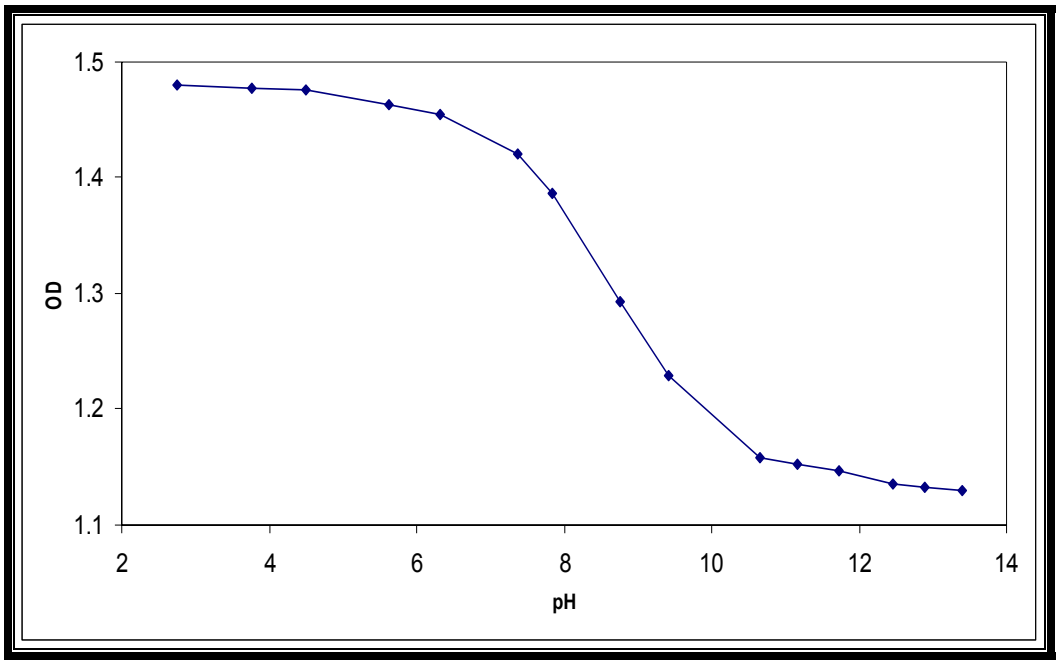
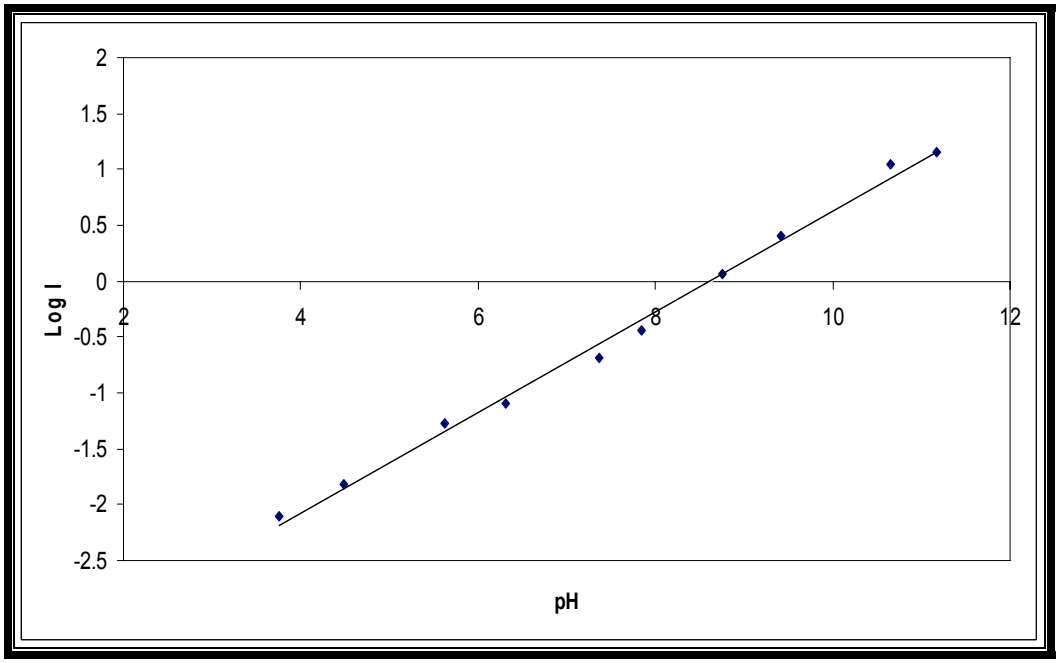


Figure 3.7.2: The plot of log I versus pH for CP-01.



REFERENCES

[1] J. B. Hansen, O. Hafliger; Determination of the dissociation constant of a weak acid using a dissolution rate method, *J. Pharma. Sci*., ***72,*** *429-31 (1983).*

[2] N. A. Kovach, O. P. Shvaika; "Applicability of some methods for determining the dissociation constants of organic electrolytes using the Fuoss-Kraus method", Deposited Doc. (VINITI 4552-84), *13 pp. (1984).*

[3] M. Uhrova, I. Miksik, Z. Deyl, S. Bellini; Determination of dissociation constants by separation methods (HPLC and CE). Theoretical background and guidelines for application**,** *Process Control Quality*., ***10,*** *151-67 (1997).*

[4] J. P. Mercier, P. Morin, Dreux, A. Tambute; "Determination of weak (2.0-2.5) dissociation constants of non-UV absorbing solutes by capillary electrophoresis"**,** *Chromatographia*., ***48,*** *529-34 (1998).*

[5] L. Fielding; NMR methods for the determination of protein-ligand dissociation constants. *Prog. in NMR Spect*., ***51,*** *219-42 (2007).*

[6] H. Tanaka, K. Aritsuka, T. Tachibana, H. Chuman, P. K. Dasgupta; "Determination of dissociation constants of weak acids by feedback-based flow ratiometry", *Analytica Chimica Acta*., ***499,*** *199-204 (2003).*

[7] M. Meloun, D. Burkonova, T. Syrovy, A. Vrana; Thermodynamic dissociation constants of silychristin, silybinin, silydianin and mycophenolate by the regression analysis of spectrophotometric data, *Analytica Chimica Acta*., ***486,*** *125-41 (2003).*

[8] A. Lachenwitzer, N. Li, J. Lipkowski; Determination of the acid dissociation constant for bisulfate adsorbed at the Pt(111) electrode by subtractively normalized interfacial Fourier transform infrared spectroscopy, *J. Electroanal. Chem*., ***532,*** *85-98 (2002).*

[9] H. S. Harmed and B. B. Owen, "The Phy. Chemistry of Electrolytic Solutions", (1958).

[10] H. A. Krebs and J. C. Speakman; "Dissociation constant, solubility, and the pH value of the solvent." *J. Chem. Soc., 593-5 (1945).*

[11] R. J. Gillespie and C. Solomons; "Solutions in sulfuric acid.-Conductivity measurements on some nitro compounds." *J. Chem. Soc.,1796-803 (1957).*

[12] H. M. Dawson, G. V. Hall and A. Key; "Acid and salt effects in catalyzed reactions.-Variation of the catalytic activity of an acid with its concentration and the determination of ionization constants." *J. Chem. Soc., 2844-53 (1928).*

[13] R. C. Farmer and F. J. Warth; "The Affinity Constants of the Aniline and its Derivatives." *J. Chem. Soc.,* ***85****, 1713-26 (1904).*

[14] A. Albert and E. P. Serjeant; "The determination of ionization constants" Chapman and Hall Ltd.: London (1984)

[15] C. Ogretir, S. Yarligan and S. Demirayak; "Spectroscopic determination of acid dissociation constant of some biologically active 6-phenyl-4, 5-dihydro-3(2H)-pyridazinone derivatives." *J. Chem. Eng. Data,* ***47(6)****, 1396-1400 (2002).*

[16] A. Niazi, A. A. Rezaei and F. Shahhosseini; "Spectrophotometric study of acidity constants of Alizarine Red S in various water-organic solvent." *Annali di Chimica*, ***97(3-4)**, 199-211 (2007).*

[17] A. Niazi, A. Yazdanipour, J. Ghasemi, A. Amini, S. Bozorgzad and M. Kubista; "Spectrophotometric investigation of the acidity constants of fluorescein in various water-organic solvent media." *Chem. Eng. Comm.*, ***195(10)**, 1257-68 (2008).*

[18] M. Pryszczewska, T. Lipiec; "Spectrophotometric determination of the dissociation constant of a complex compound", *Roczniki Chemii., **29**, 985-92 (1955).*

[19] Z. L. Ernst, J. Menashi; "Spectrophotometric determination of the dissociation constants of some substituted salicylic acids", *Tran. Farad. Soc., **59**, 230-40 (1963).*

[20] I. I. Hewala, F. A. el-Yazbi, A. Awad, A. M. Wahbi; "Determination of dissociation constants of some pharmaceutical compounds using derivative spectrophotometry", J. Clin. Pharm. Thera., **17**, 233-39 (1992).

[21] M. Kadar, A. Biro, K. Toth, B. Vermes, P. Huszthy; "Spectrophotometric determination of the dissociation constants of crown ethers with grafted acridone unit in methanol based on Benesi-Hildebrand evaluation", *Spectrochim. Acta, Part A: Mol. Biomol. Spect.*, **62,** 1032-38 (2005).

[22] V. L. Cherginets, O. V. Demirskaya and T. P. Rebrova; "Potentiometric study of acid-base equilibria in the {KCl + LiCl} eutectic melt at temperatures in the range (873 to 1073) K." *J. Chem. Thermodynamics*, ***36(2)**, 115-20 (2004).*

[23] A. Dogan and E. Kilic; "Tautomeric and microscopic protonation equilibria of some α -amino acids." *Anal. Biochem.*, ***365(1)**, 7-13 (2007).*

[24] M. Taha; "Thermodynamic study of the second-stage dissociation of N,N-bis-(2-hydroxyethyl)glycine (bicine) in water at different ionic strength and different solvent mixtures." *Annali di Chimica, **94(12)**, 971-78 (2004).*

[25] H. Zhao, L. Yuan and L. Wang; "Quantitative Structure-Activity Relationships of Organic Acids and Bases." *Bull. Environ. Contam. Toxicol., **57,** 242-49 (1996).*

[26] H. Rochester; " Acidity Functions" *Academic Press: New York, (1971).*

[27] L. Hammet; "Physical Organic Chemistry" *Mc Graw – Hill; New York, (1940).*

[28] P. Hagenmuller; "New method of determination of the dissociation constant of a complex in solution"**,** *Compt. rend., **230**, 2190-92 (1950).*

[29] V. P. Vasil'ev; "Effect of ionic strength on the dissociation constants of complex compounds", *Zhur. Neorga. Khim., **7**, 1788-94 (1962).*

[30] C. Patel and R. Patel; "Acid dissociation constants of some 3-substituted 2-hydroxy-5-methylacetophenones and the formation constants of their metal complexes", *J. Ind. Chem. Soc., **52**, 312-14 (1975).*

[31] J. F. Morrison, W. W. Cleland; "A kinetic method for determining dissociation constants for metal complexes of adenosine 5'-triphosphate and adenosine 5'-diphosphate", *Biochem. **19**, 3127-31 (1980).*

[32] U. Piran, W. J. Riordan; "Dissociation rate constant of the biotin-streptavidin complex", *J. Immuno. Methods., **133,** 141-43 (1990).*

[33] B. Sandra, H. Alka, M. Pavlovic and D. Kastelan; "Determination of pKa values of active pharmaceutical ingredients." *Trends in Anal. Chem., **26(11),** 1043-1061(2007).*

[34] J. Satchell and B. Smith; "Calculation of aqueous dissociation constants of 1,2,4-triazole and tetrazole: A comparison of solvation models." *Phy. Chem. Chem. Phy., **4(18),** 4314-4318 (2002).*

[35] S. Alexander, R. Giorgio; "Dissociation of polyvalent electrolytes." *J. Chromato., **853(1+2),** 35-44 (1999).*

[36] G. Gonzalez and A. Herrador, A. "Acid-base behavior of some substituted azo dyes in aqueous N,N-dimethylformamide mixtures." Agustin; *Anal. Chim. Acta, **246(2),** 429-34 (1991).*

[37] N. Sachan, C. Chandel, M. Gupta; "Determination of microscopic dissociation constants of some tetracyclines." *J. Electrochem. Soc. Ind., **31(3),** 1-4 (1982).*

[38] E. Reardon; "Dissociation constants for alkali earth and sodium borate ion pairs from 10 to 50° C." *Chem. Geology., **18(4),** 309-25 (1976).*

[39] J. Shukla, R. Sharma and M. Patil; "Proton dissociation constants of benzoylacetone and isonitrosobenzoylacetone in aqueous dioxane media." *Monatshefte fuer Chemie, **118(8-9),** 931-46 (1987).*

[40] J. Partanen, P. Juusola and V. Verraes; "Re-evaluation of the second thermodynamic dissociation constants of α -alanine, valine, and leucine using potentiometric data measured for aqueous potassium chloride solutions at 298.15 K." *Can. J. Chem., **83(1),** 46-56 (2005).*

[41] C. Lopez, D. Ibrahim, F. Antonio, M. Howard and M. Masaaki; "Base strengths of substituted tritylamines, N-alkylanilines, and tribenzylamine in aqueous solution and the gas phase: Steric effects upon solvation and resonance interactions." *Eur. J. Org. Chem., **(24),** 5031-39 (2004).*

[42] V. Evagelou, A. Tsantili and M. Koupparis; "Determination of the dissociation constants of the cephalosporins cefepime and cefpirome using UV spectrometry and pH potentiometry." *J. Pharma. Biomed. Anal.,**31(6)**, 1119-28 (2003).*

[43] M. Kadar, A. Biro, K. Toth, B. Vermes and P. Huszthy; "Spectrophotometric determination of the dissociation constants of crown ethers with grafted acridone unit in methanol based on Benesi-Hildebrand evaluation." *Spectrochim. Acta, **62A(4-5)**, 1032-38 (2005).*

[44] J. A. Riddick, W. B. Bunger and T. Sakano; Organic solvents-Physical properties and Methods for purification, **4th Edition**, Techniques of Chemistry, ***Vol.II**, Wiley/interscience, Wiely, New York (1986).*

[45] Sawyer, Heineman and Beebe; Chemistry Experiments for Instrumental Analysis, *Wiley, New York, 6-4(1984).*

[46] Skoog, Holler and Nieman; "Principles of Instrumental Analysis" *5th edition, 13-14, (1998).*

[47] C. Ogretir, H. Dal, H. Berber and F. Taktak; "Spectroscopic Determination of Acid Dissociation Constants of Some Pyridyl Shiff Bases" *J. Chem. Eng. Data,* ***51,*** *46-50 (2006)*

[48] C. Ogretir, S. Demirayak and N. T. Funda; "Spectroscopic determination of acid dissociation constant of some pyridyl-substituted 2-aminothiazole derivatives" *J. Chem. Eng. Data,* ***51(3)****, 946-51 (2006).*

[49] H. Berber, C. Ogretir and E. Ermis; "Spectroscopy determination of acidity constant of some monoazo resorcinol derivative." *J. Chem. Eng. Data,* ***53(5)****, 1049-55 (2008).*

INTRODUCTION

The discovery of antimicrobials like penicillin and tetracycline provide the noble way for better health for millions of people around the world. Before its invention in the early 1940's, there was no true cure for gonorrhea, strep throat or pneumonia like diseases. Now, most of these infections can be cured easily with a short course of antimicrobials.

However, the effectiveness of antimicrobial drugs now days available in market are somewhat in doubt in future because microorganisms, especially bacteria, are becoming resistant to more and more antimicrobial agents. It leads to the discovery of new antimicrobial agents. However, microorganisms are becoming resistant more quickly than new drugs are being made available. So, today's need is to overcome resistance to antimicrobials or to treat infections with alternative means. To fulfill this demand, various compounds are synthesized and screened for its antimicrobial activity. QSAR (Quantitative structure-activity relationship) is one of the best way for the prediction of biological activity of the structure prior to its synthesis and finally to syntheses more active compounds by structure modification of known antimicrobial agents [(1-3)].

The process of drug discovery involves the design of moiety, synthesis, characterization, screening, and assays for therapeutic efficacy. So, the study of antimicrobial activity of various compounds is one of the important phase for the discovery of new microbial active agents. Literature survey shows that benzoquinoline moiety exhibited biological activity[(4-8)]

This chapter describes the study of antimicrobial activity of synthesized cyanopyridines, aminopyrimidines, 1, 5-benzodiazepines, pyrazolines and sulphonamides. All these compounds contain the same benzo[h]quinoline moiety. The screening was done against some Gram positive and Gram negative bacteria as well as against some fungal strains. The study was done in DMSO and DMF.

EXPERIMENTAL

The antibacterial and antifungal activities of all synthesized compounds were studied in DMSO and DMF, which were purified by standard procedure[9]. All the synthesized compounds were recrystallized prior to use.

For all the compounds, agar well diffusion method was used.

Test Microorganisms:

The synthesized compounds were tested against Gram positive bacteria viz. *Staphylococcus aureus* ATCC 25923, *Bacillus megaterium* ATCC9885, Gram negative bacteria viz. *Klebsiella pneumoniae* NCIM2719 and *Proteus mirabilis* NCIM2241 and for antifungal activity *Candida tropicalis* ATCC4563 was used.

All the strains were obtained from National Chemical Laboratory (NCL), Pune, India and were maintained at 4°C on nutrient agar slants (for bacteria) and MGYP slant (For fungi).

Preparation of test compounds:

The solutions were prepared at a concentration of 20 mg/ml for all the compounds.

Preparation of the plates and microbiological assay:

The antibacterial evaluation was done by agar well diffusion method[10] using Mueller Hinton agar No. 2 (for bacteria) and Sabroad dextrose agar (for fungi) as the nutrient medium. The agar well diffusion method was preferred to be used in this study because it was found to be better than the disc diffusion method as suggested by Parekh et al. [11] The bacterial strains were activated by inoculating a loop full of test strain in 25 ml of N-broth and the same was incubated for 24 h in an incubator at 37^{o} C. 0.2 ml of the activated strain was inoculated in molten agar. Mueller Hinton Agar kept at 45^{o}C was then poured in the Petri dishes and allowed to solidify. After solidification of

the media, 0.85 cm ditch was made in the plates using a sterile cork borer and these were completely filled with the test solution (2mg/ml) . The plates were incubated for 24 h at 37^{o}C. The mean value obtained for the three wells was used to calculate the zone of growth inhibition of each sample. The controls were maintained for each bacterial strain and each solvent. The inhibition zone formed by these compounds against the particular test bacterial strain determined the antibacterial activities of these synthesized compounds.

RESULTS AND DISCUSSION

Cyanopyridines

Figure 4.1 shows inhibition against Gram positive bacteria in both DMSO and DMF. For both Gram positive bacteria, CP-6 exhibited maximum inhibition in both the solvents. Against *S. aureus*, in DMSO CP-5 and CP-7 and in DMF, CP-7 showed no inhibition at all. For *B. megaterium*, only CP-1, CP-2, CP-3, CP-4 and CP-6 exhibited inhibition in DMSO. Other compounds had no effect at all. In DMF, except CP-7 all compounds showed inhibition against *B. megaterium*.

The inhibition depends upon three S: strain, solvent and structure. All the compounds have the same central moiety but different side chains. So, presence of different side chain affects inhibition in the studied compounds. CP-6 contains m-hydroxy group which is most effective in comparison to other groups.

Comparison of inhibition in both the solvents shows that inhibition is more in DMF than in DMSO. So, for Gram positive bacteria, DMF is good solvent. In DMSO *B. megaterium* is most resistant bacteria.

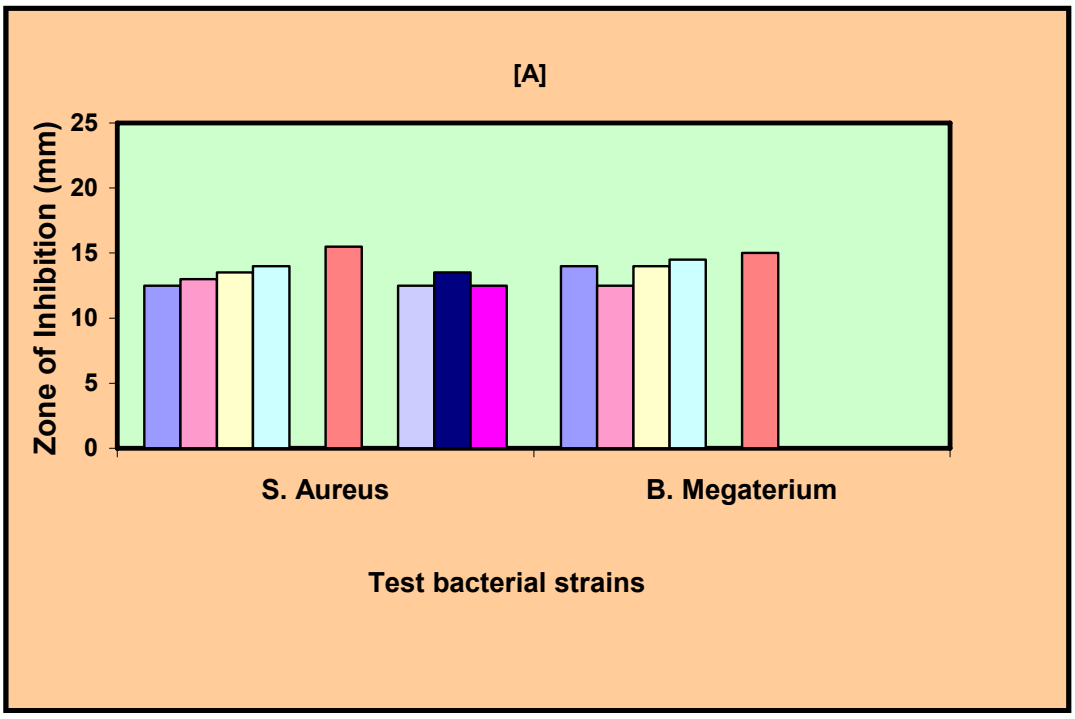
Figure 4.2 shows zone of inhibition against Gram negative bacteria in DMSO and DMF for the studied compounds. Again, inhibition is maximum for CP-6 in both the solvents against *K. pneumoniae* and *P. mirabilis.* In DMSO, CP-7 showed no inhibition against *K. pneumoniae* and *P. mirabilis*. However, in DMF CP-7 and CP-8 for *K. pneumoniae* and CP-5 against *P. mirabilis* exhibited no inhibition.

Thus, for Gram negative bacteria also, m-hydroxy substitution is most effective in both the solvents. Whereas p-nitro (as in CP-5), p-chloro (as in CP-7) and m-nitro (as in CP-8) had no effect on studied Gram negative bacteria.

Further, for Gram negative bacteria, inhibition is more in DMSO than in DMF. So, DMSO is better solvent for the studied Gram negative bacteria.

Figure 4.3 shows zone of inhibition against fungal strain *C. tropicalis.* In DMSO, CP-2 and in DMF, CP-6 exhibited more inhibition. CP-7 had no effect in DMSO whereas in DMF both CP-5 and CP-7 showed no effect at all.

Figure 4.1: Antibacterial activity of cyanopyridines against Gram positive bacteria in [A] DMSO and [B] DMF.



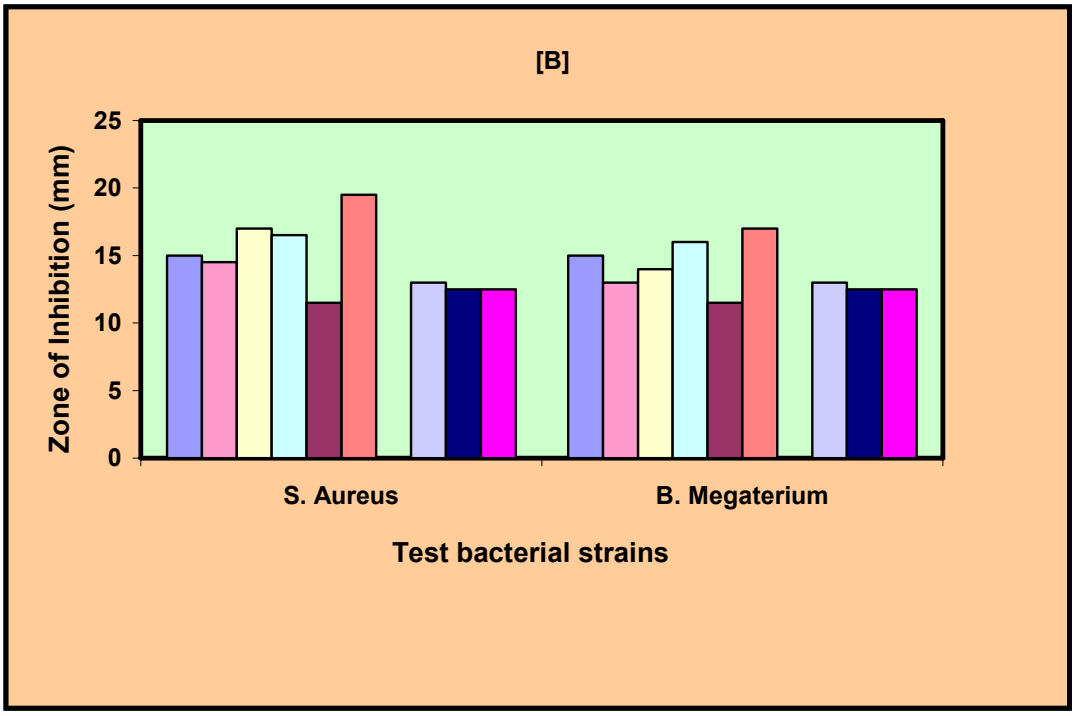
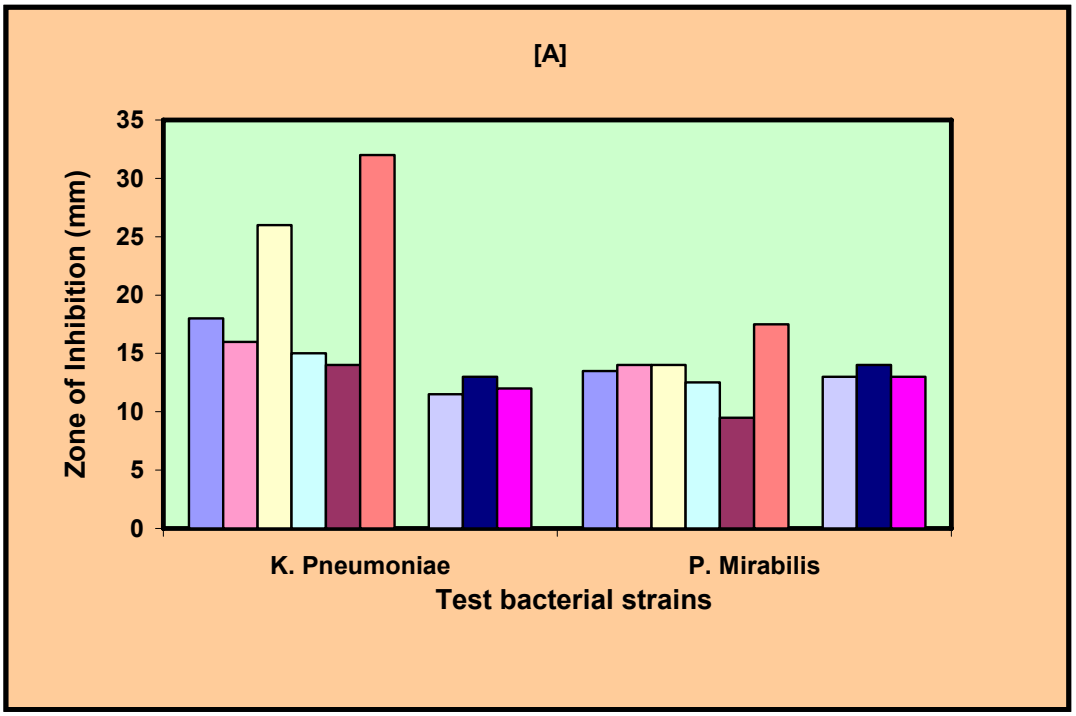


Figure 4.2: Antibacterial activity of cyanopyridines against Gram negative bacteria in [A] DMSO and [B] DMF.

CP-1, CP-2, CP-3, CP-4, CP-5, CP-6, CP-7, CP-8, CP-9, CP-10



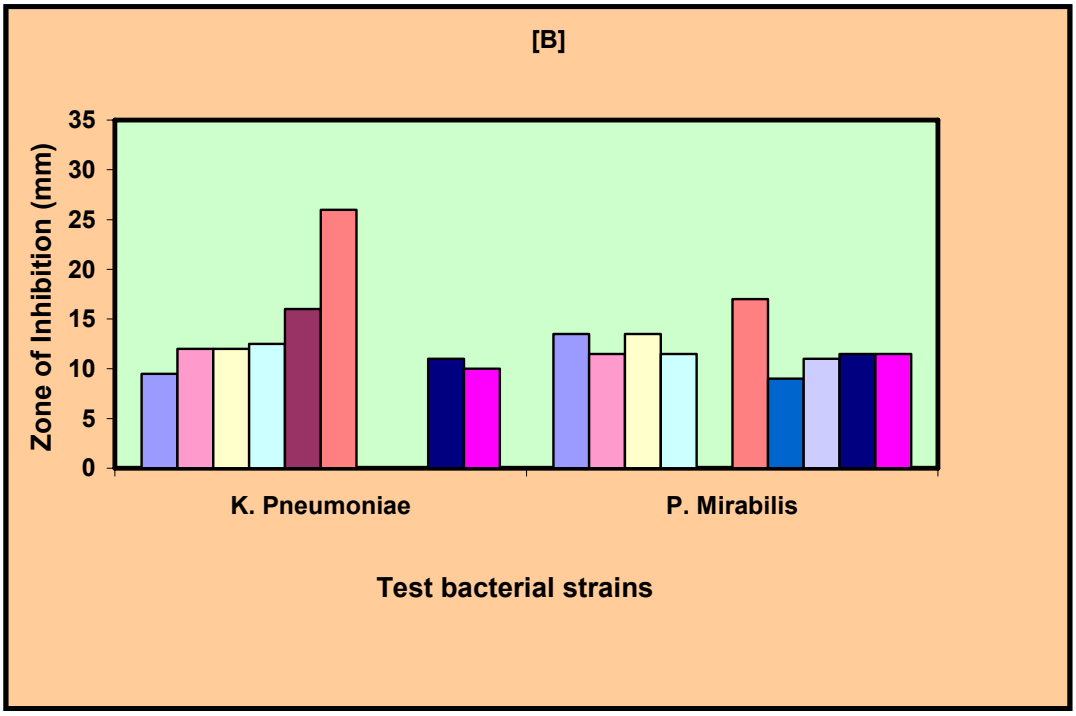
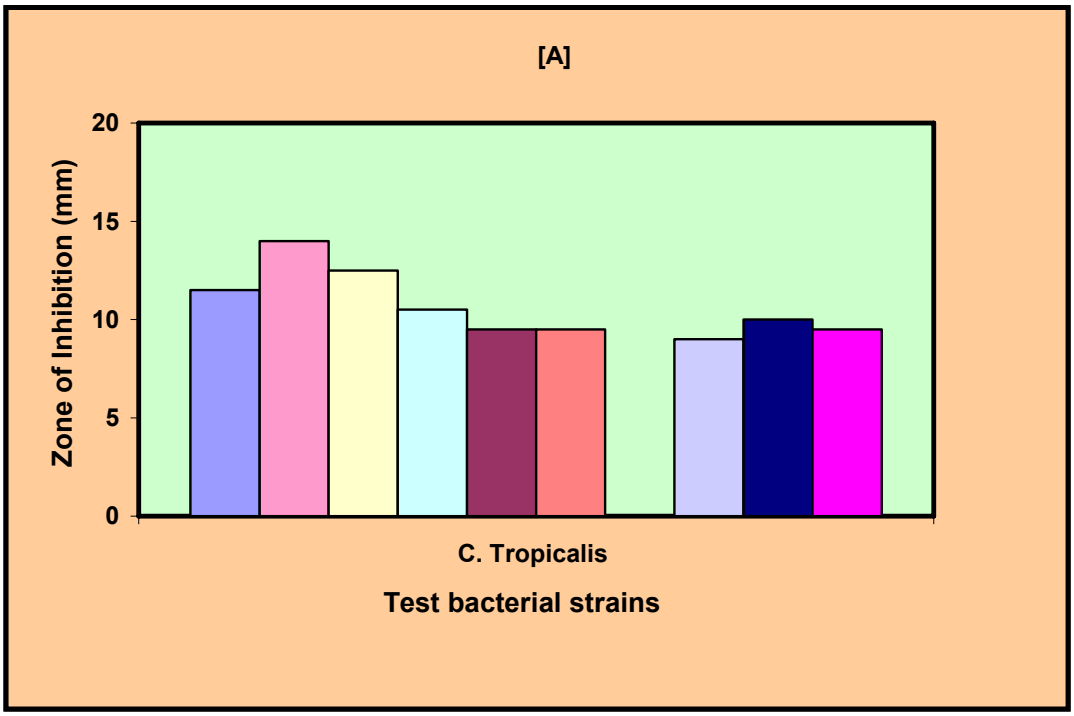
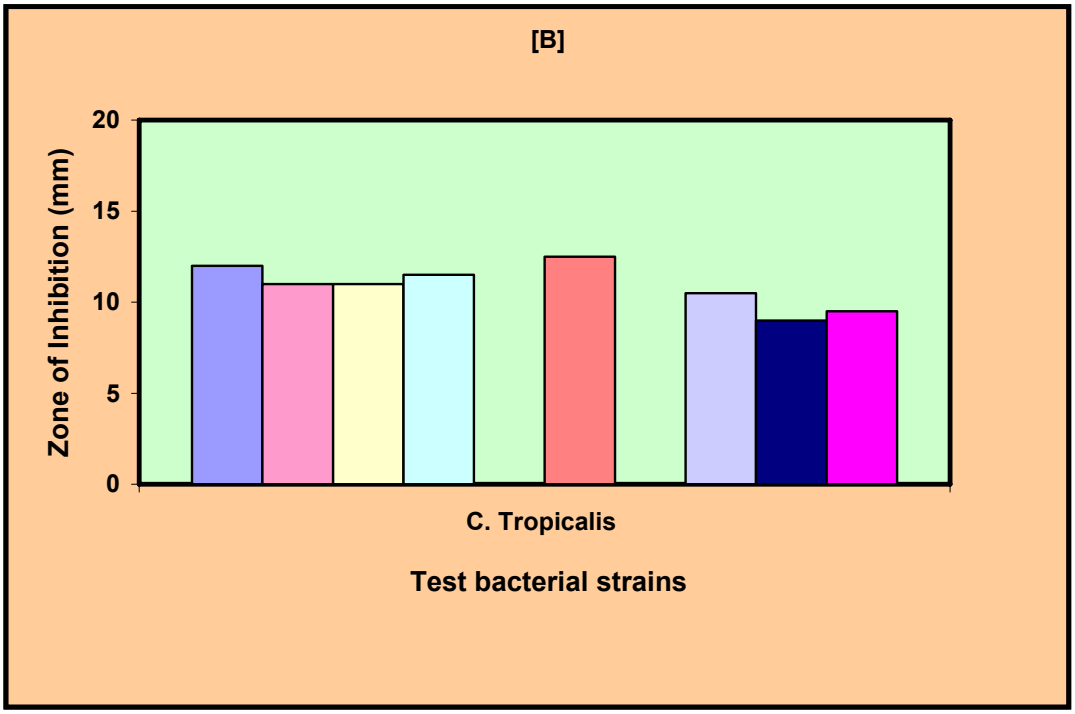


Figure 4.3: Antifungal activity of cyanopyridines in [A] DMSO and [B] DMF.

CP-1, CP-2, CP-3, CP-4, CP-5, CP-6, CP-7, CP-8, CP-9, CP-10





Thus, in DMSO, p-methyl (as in CP-2) and in DMF m-hydroxy (as in CP-6) are most effective.

Overall, DMF showed higher inhibition for the studied fungal strain than DMSO.

Aminopyrimidines

Figure 4.4 shows zone of inhibition against Gram positive bacteria in both DMSO and DMF. It is observed that in DMF against both S. aureus and *B. megaterium,* except JRM-1, all the compounds showed inhibition whereas in DMSO, JRM-1, JRM-5 and JRM-6 are not effective at all. In both DMSO and DMF, JRM-9 showed maximum inhibition.

JRM-9 contains p-hydroxy group which is found to be most effective in both DMSO and DMF for these Gram positive bacteria. Overall, DMF is good solvent for the studied Gram positive bacteria.

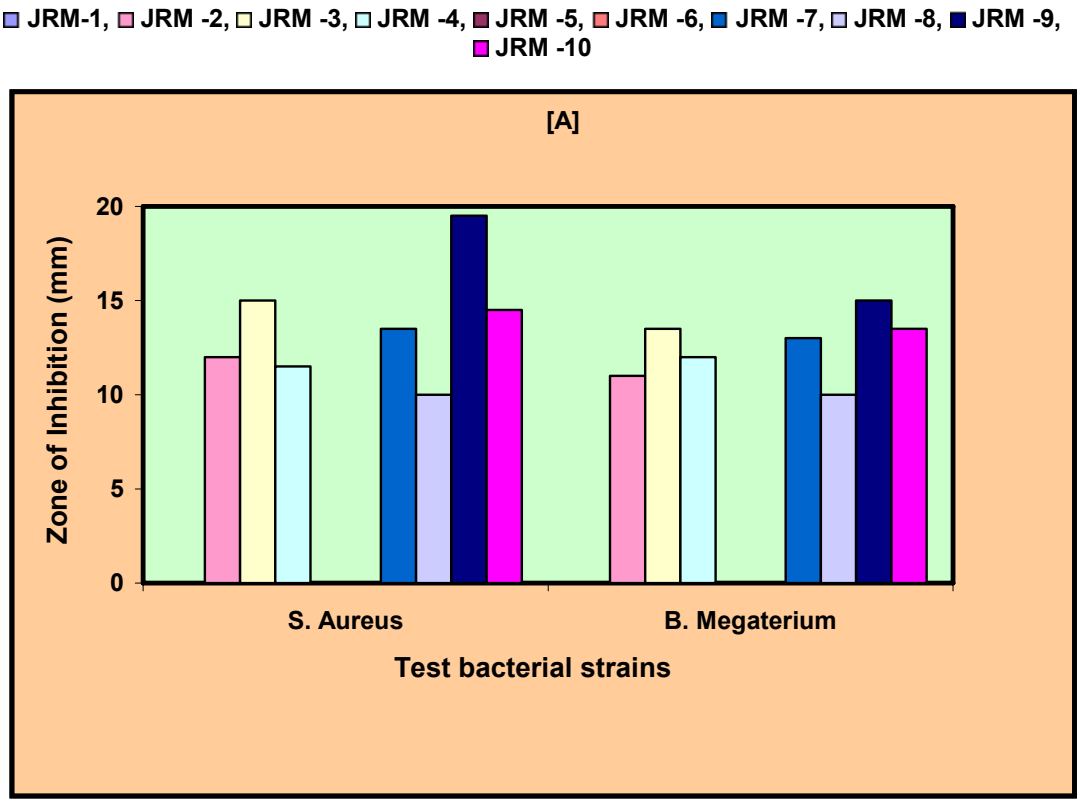
The zone of inhibition against Gram negative bacteria is shown in Figure 4.5 for both DMSO and DMF. Again, in DMF, most of the compounds exhibit inhibition. In DMF. against *K. Pneumoniae*, JRM-1 and JRM-4 showed no inhibition and maximum is observed for JRM-2. Whereas against *P. mirabilis* all compounds showed inhibition and JRM-5 showed maximum

inhibition. Thus, p-methyl group is most effective against *K. Pneumoniae* whereas p-hydroxy causes maximum inhibition against *P. mirabilis.* In DMSO, against *K. Pneumoniae*, JRM-1, JRM-5 and JRM-6 showed no activity and JRM-9 exhibited maximum inhibition. For *P. mirabilis*, further JRM-1 failed, whereas JRM-9 shows maximum inhibition. Thus, the presence of p-hydroxy (as in JRM-9) increases the inhibition against both the Gram negative bacterial strains in DMSO.

Figure 4.6 shows zone of inhibition against *C. tropicalis* fungi in DMSO and DMF. Again, in DMSO, JRM-9 is most effective whereas JRM-6 showed minimum inhibition. JRM-1 did not affect the studied fungi. In DMF, JRM-5 is most effective, whereas JRM-1 and JRM-6 showed equally minimum inhibition. Further, all the compounds showed inhibition against the studied fungi *C. tropicalis*. Thus, in DMSO p-hydroxy is most effective whereas in DMF, p-nitro is highly effective.

Thus, in this series of compounds, solvent and substitution play an important role in inhibition. Against both Gram positive and Gram negative bacteria and fungal strain, DMF is found to be good solvent.

Figure 4.4: Antibacterial activity of aminopyrimidines against Gram positive bacteria in [A] DMSO and [B] DMF.



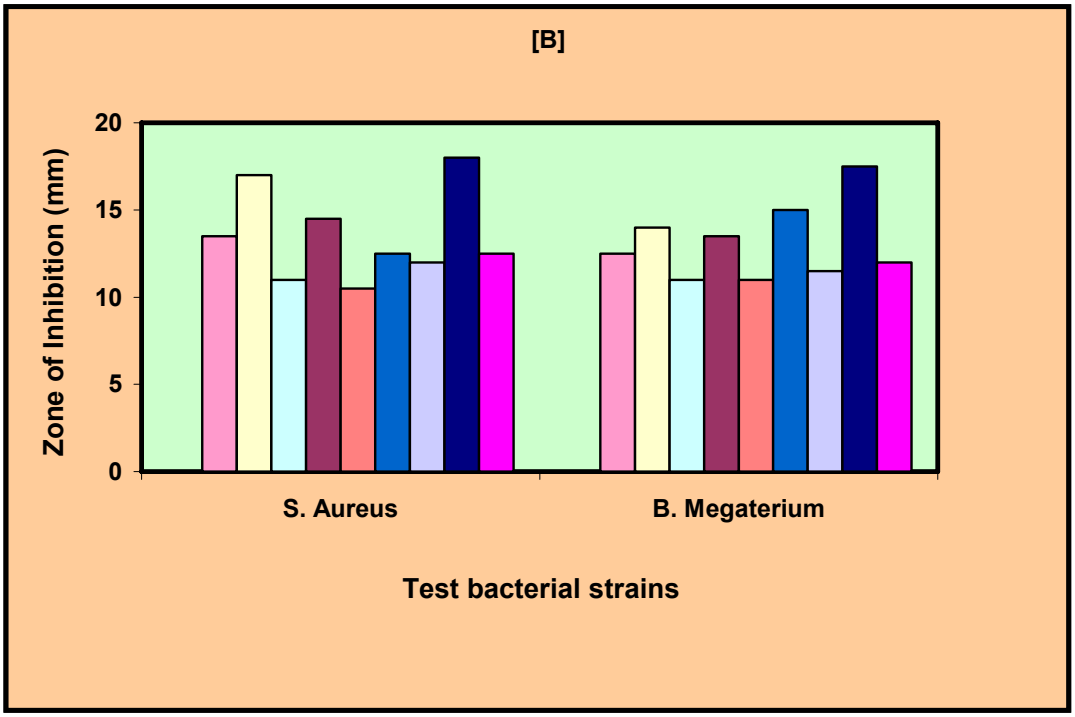


Figure 4.5: Antibacterial activity of aminopyrimidines against Gram negative bacteria in [A] DMSO and [B] DMF.

JRM-1, JRM -2, JRM -3, JRM -4, JRM -5, JRM -6, JRM -7, JRM -8, JRM -9, JRM -10

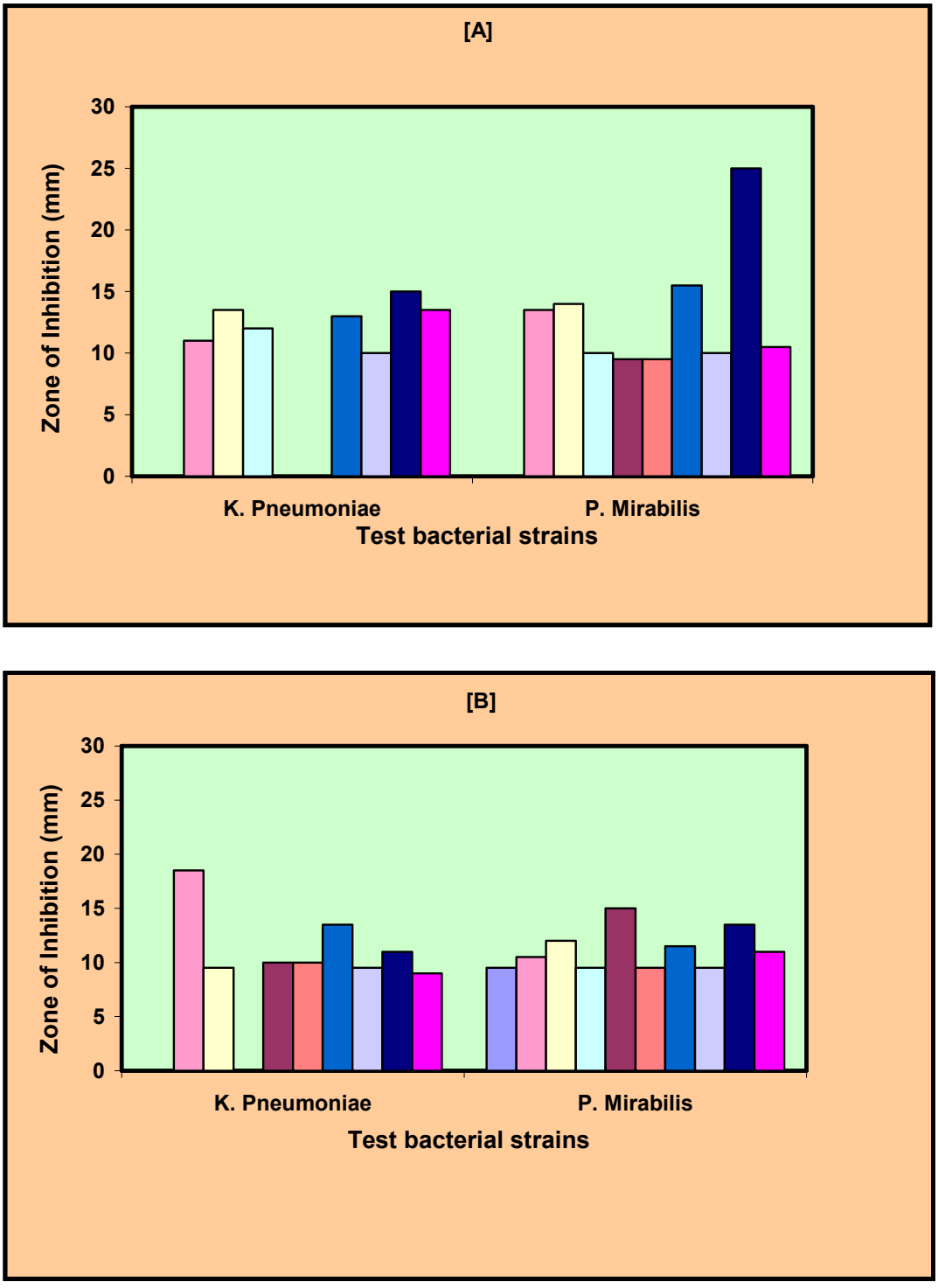
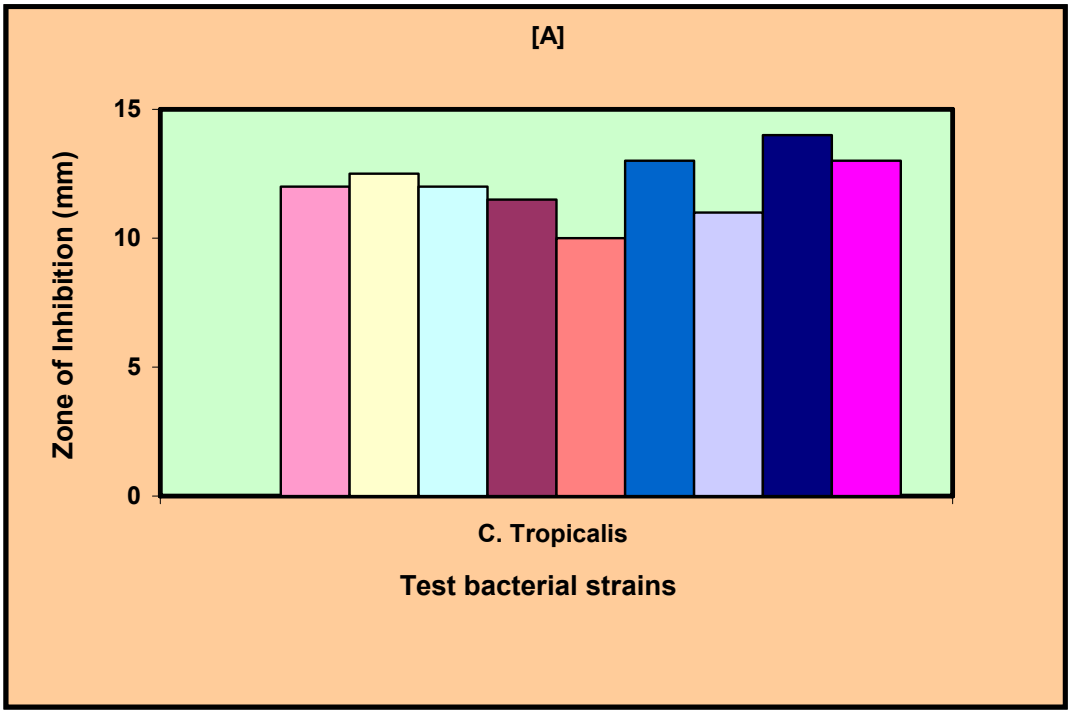
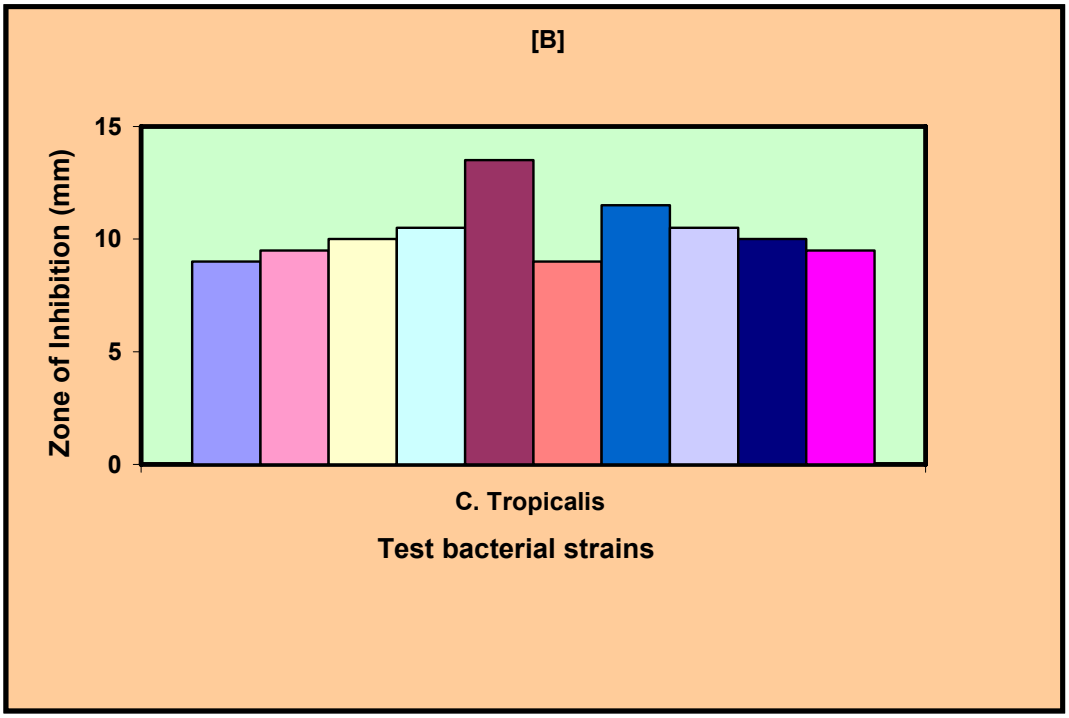


Figure 4.6: Antifungal activity of aminopyrimidines in [A] DMSO and [B] DMF.

JRM-1, JRM -2, JRM -3, JRM -4, JRM -5, JRM -6, JRM -7, JRM -8, JRM -9, JRM -10





1, 5 benzodiazepines

Figure 4.7 shows the inhibition against Gram positive bacteria in DMSO and DMF. It is observed that against both *S. aureus* and *B.*

megaterium, all the compounds except MRV-8 exhibited inhibition in both the solvents. In DMSO, MRV-2 showed maximum inhibition and MRV-3 showed minimum inhibition against both Gram positive bacteria. In DMF also, against *S. aureus,* MRV-2 shows maximum inhibition whereas MRV-3 had minimum inhibition. Against, *B. megaterium,* MRV-6 exhibited maximum inhibition whereas MRV-9 showed minimum inhibition.

The inhibition depends on the solvent, compound structure (i.e., substitution) and bacterial strain. Thus, in DMSO p-methyl group (as in MRV-2) is most effective whereas p-bromo group (as in MRV-3) is least effective for both studied bacterial strains. In DMF, for *S. aureus,* p-methyl group (in MRV-2) is most effective whereas p-bromo group (in MRV-3) is least effective but against *B. megaterium,* m-hydroxy is found to be more effective because MRV-6 exhibited maximum inhibition.

MRV-8 contains m-nitro group which is not effective at all for the studied Gram positive bacteria in both the solvents.

Figure 4.8 shows zone of inhibition against Gram negative bacteria in DMSO and DMF for the studied compounds. For *K. pneumoniae,* all the studied compounds showed inhibition in DMSO, among which activity is maximum for MRV-1(containing p-methoxy group) and minimum for MRV-3 (containing p-bromo group). For *P. mirabilis,* MRV-2 exhibited maximum inhibition whereas MRV-3 and MRV-7 showed equally lowest inhibition. MRV-7 shows no inhibition at all. Thus, in DMSO, p-methoxy and p-methyl groups are effective for *K. pneumoniae* and *P. mirabilis* respectively.

In DMF, MRV-6 showed maximum activity against *K. pneumoniae,* where as MRV-1 and MRV-3 exhibited no inhibition. For *P. mirabilis,* all compounds showed inhibition. Among them, MRV-6 and MRV-2 showed maximum inhibition whereas MRV-8 exhibited minimum inhibition.

Thus, in DMF compound with -OH substitution at meta position (in MRV-6) is most effective for both bacterial strains. P-methyl group present in MRV-2, is also effective for *P. mirabilis.*

Figure 4.9 shows zone of inhibition against a single fungal strain in DMSO and DMF. It is clear from figure that inhibition is more in DMF than in DMSO. In DMSO, MRV-8 exhibited no inhibition whereas MRV-3, MRV-6 and

MRV-9 showed equally maximum inhibition. In DMF, MRV-6 showed higher inhibition whereas MRV-4 showed minimum inhibition.

Thus, again for the studied fungal strain, DMF is better solvent and -OH substitution at meta position (in MRV-6) is most effective.

Figure 4.7: Antibacterial activity of 1,5-benzodiazepines against Gram positive bacteria in [A] DMSO and [B] DMF.

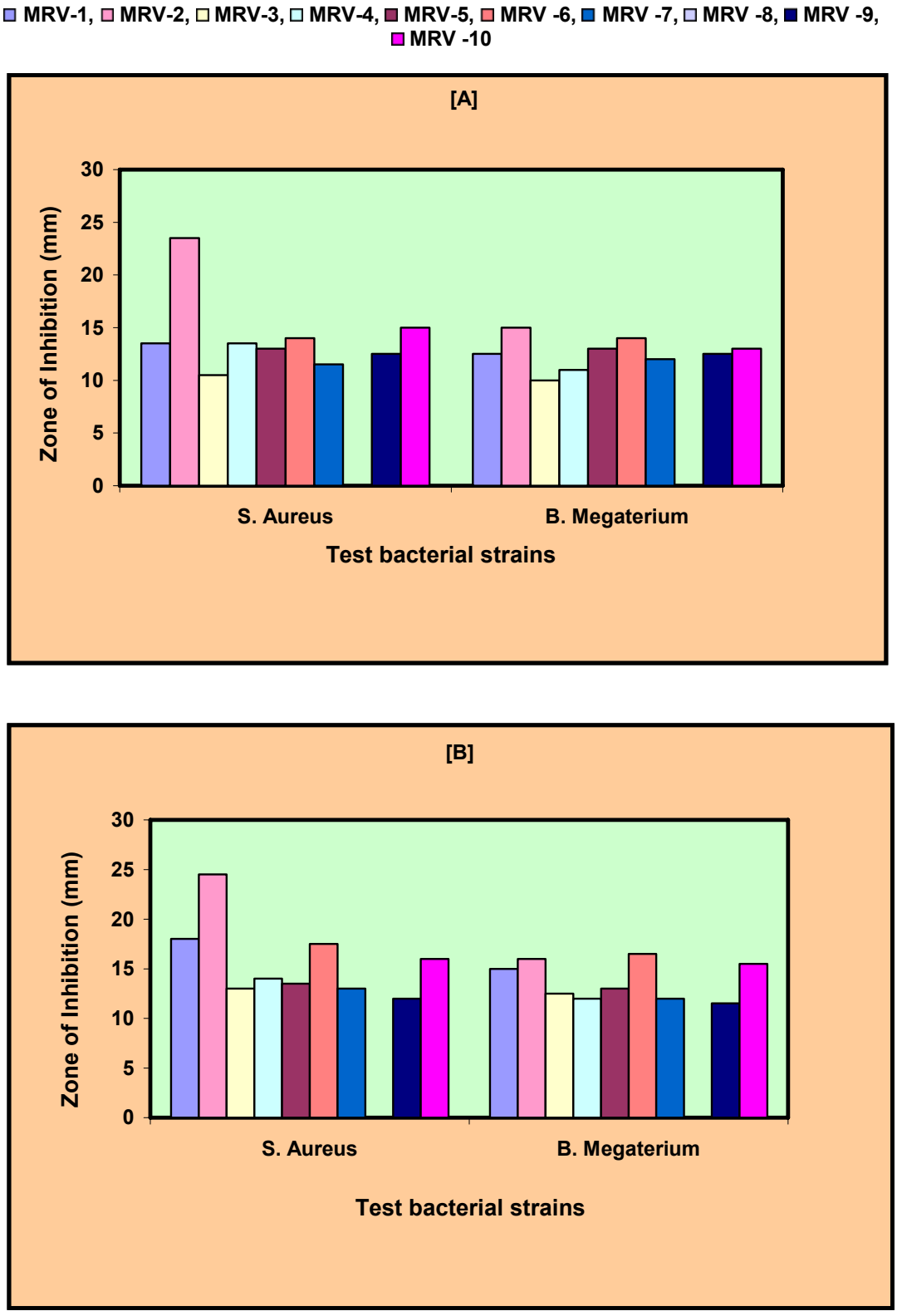


Figure 4.8: Antibacterial activity of 1,5-benzodiazepines against Gram negative bacteria in [A] DMSO and [B] DMF.

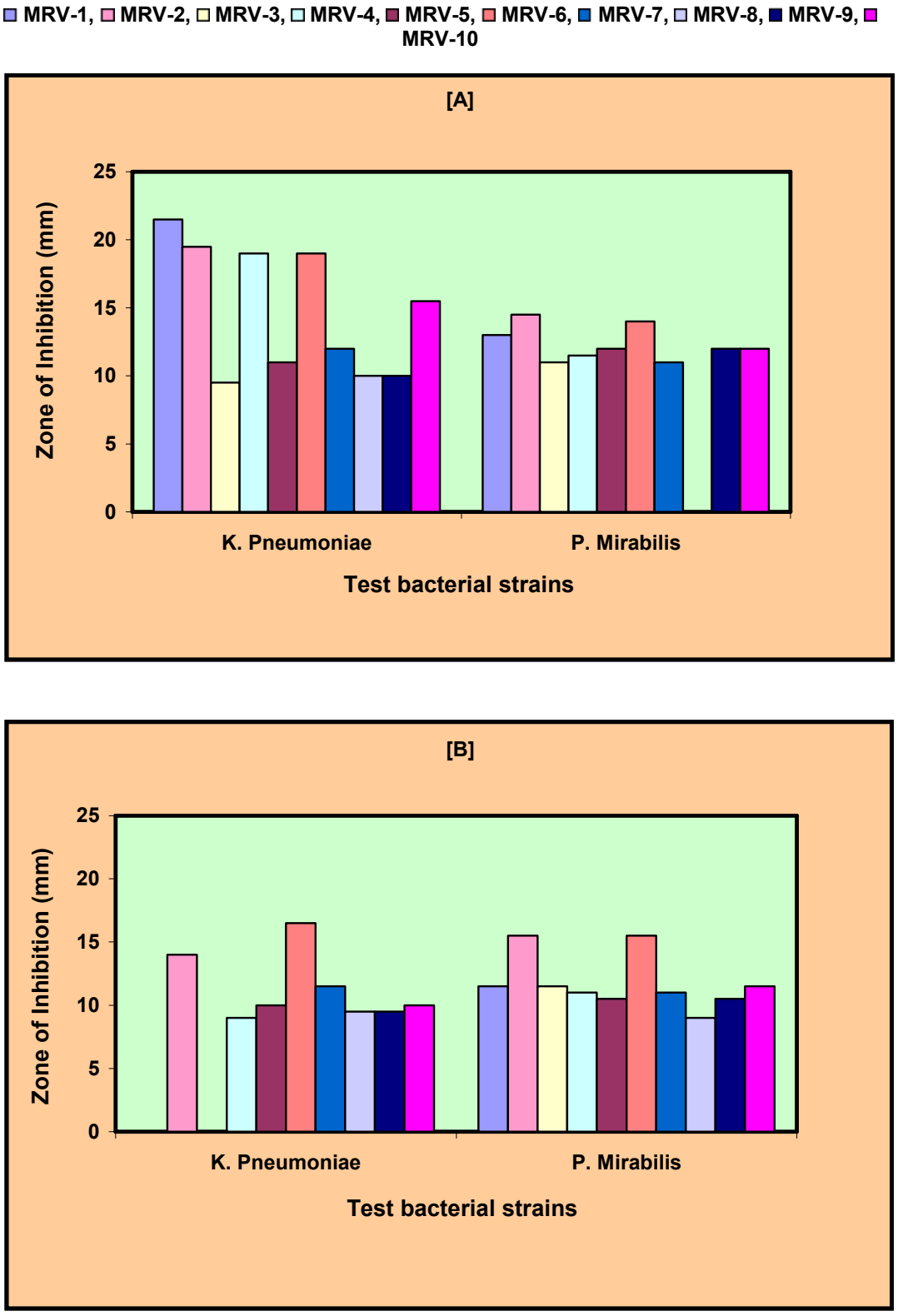
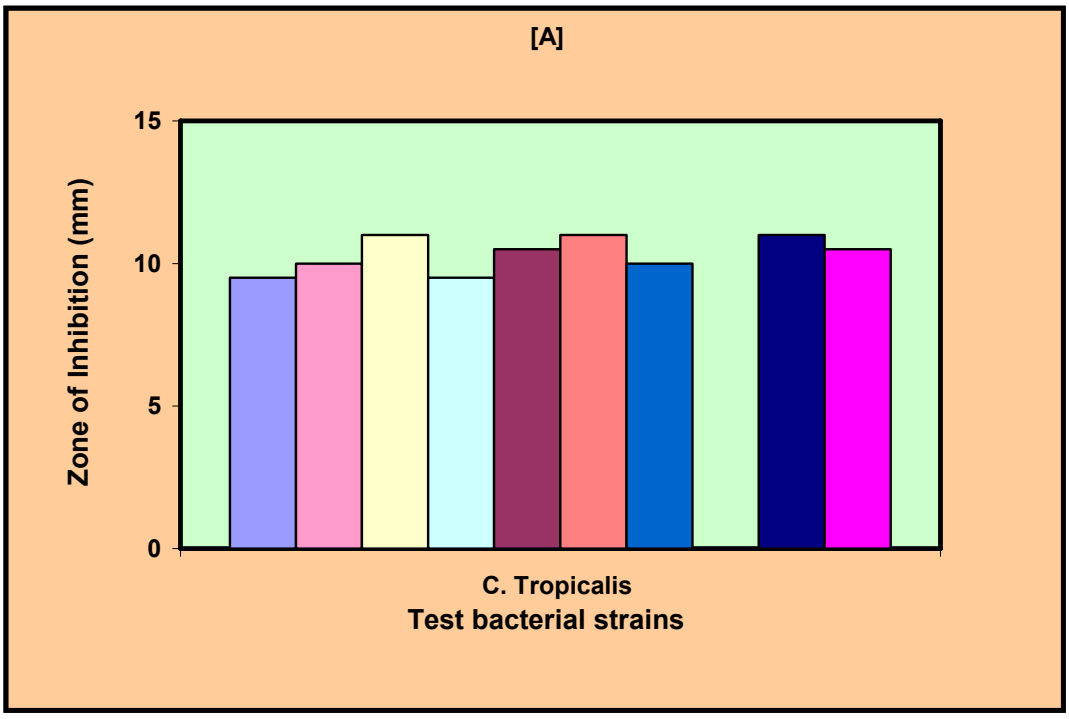
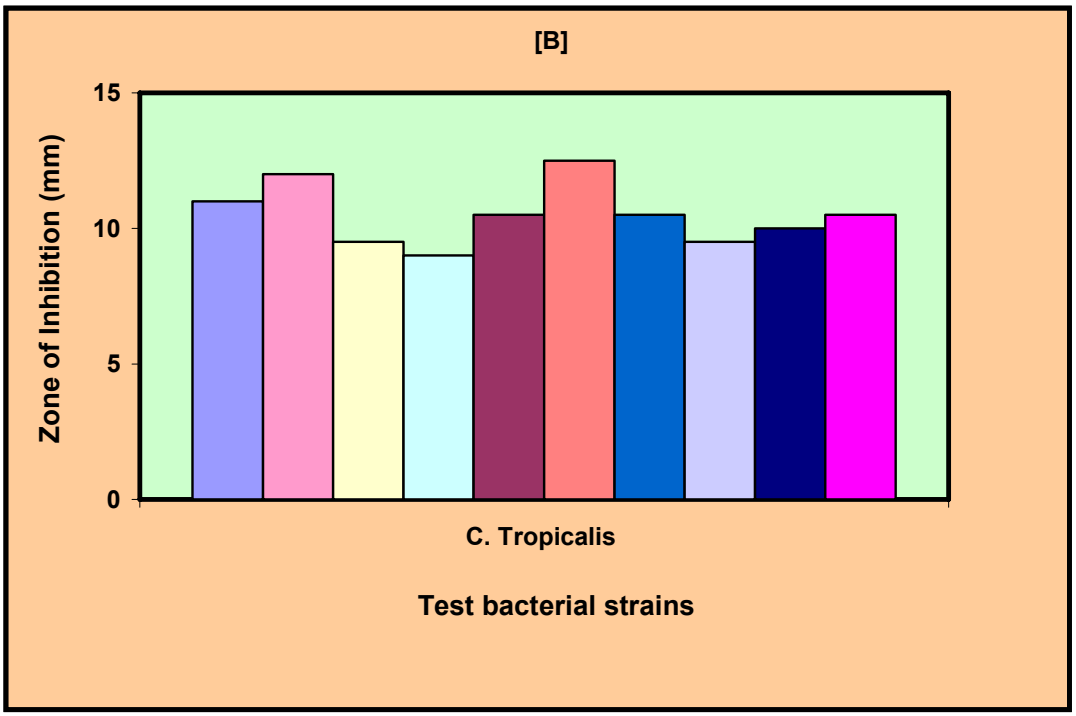


Figure 4.9: Antifungal activity of 1,5-benzodiazepines in [A] DMSO and [B]

DMF.

MRV-1, MRV-2, MRV-3, MRV-4, MRV-5, MRV-6, MRV-7, MRV-8, MRV-9, MRV-10





Pyrazolines

Figure 4.10 shows inhibition against Gram positive bacteria in DMSO and DMF. Against both the strains *S. aureus* and *B. megaterium*, JRV-1 showed maximum inhibition in DMSO. Minimum is observed for JRV-3 and JRV-4 for *S. aureus* whereas *B. megaterium,* JRV-9 showed minimum.. JRV-2 could not affect for both the strains. Thus, in DMSO, p-methoxy group is most effective for the studied bacteria.

In DMF, compound JRV-1 and JRV-10 showed equally maximum inhibition for *S. aureus,* whereas JRV-8 shows minimum inhibition. Against *B. megaterium,* JRV-1 and JRV- 7 shows equally maximum inhibition, whereas JRV-5 and JRV-9 shows equally minimum inhibition. For both bacterial strains, JRV-2 shows no inhibition at all. Thus, in DMF also, -methoxy group is most effective for the studied bacteria. Further, DMF is better solvents for the studied compounds against these two Gram positive bacteria.

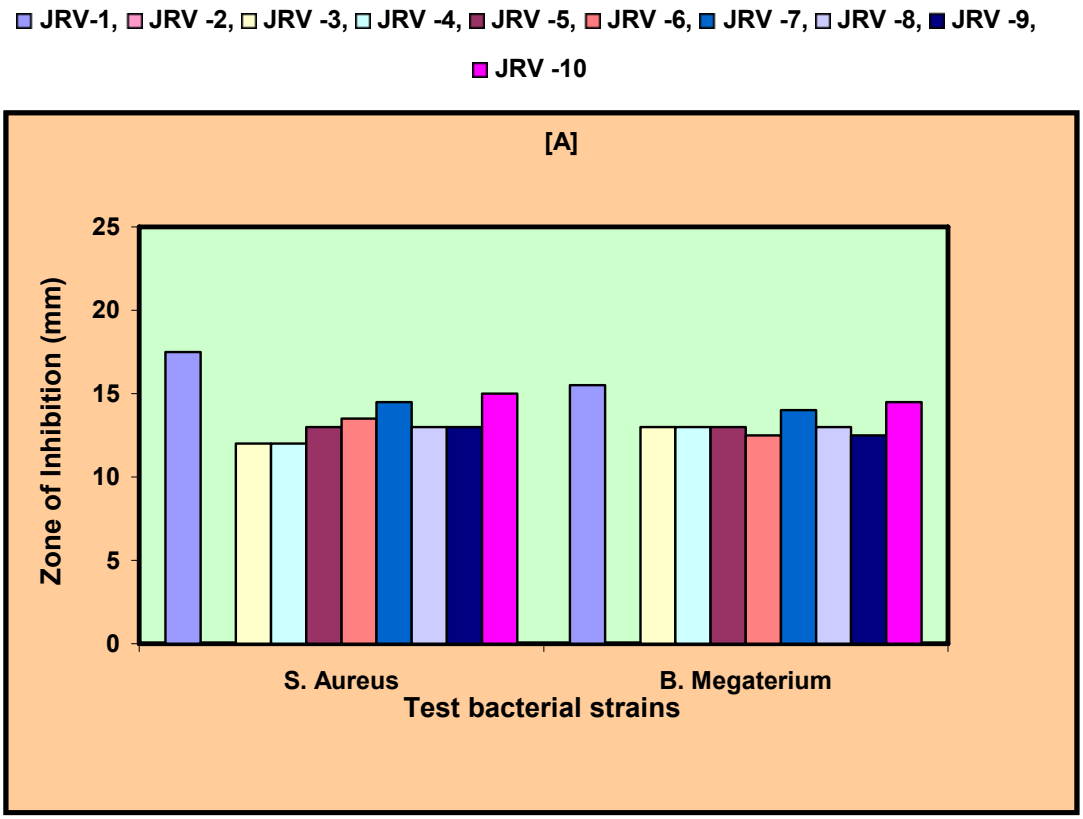
The zones of inhibition against Gram negative bacteria in DMSO and DMF are shown in Figure 4.11 for the studied compounds. Again, activity is maximum of JRV-1 for both the strains in both the solvents. In DMSO, against *K. pneumoniae,* JRV-2, JRV-9 and JRV-10 and for *P. mirabilis,* JRV-2, showed no inhibition at all. In DMF, all the studied compounds showed inhibition. For both Gram negative bacteria, inhibition is maximum for JRV-1 which is followed by JRV-10.

Thus, for Gram negative bacteria also, p–methoxy group is most effective in both the solvents.

Figure 4.12 shows zone of inhibition against a fungal strain *C. tropicalis* in DMSO and DMF. IN DMSO, all the studied compounds exhibited inhibition whereas in DMF JRV-6 had no effect at all. In DMSO, JRV-8 is most effective which contains m-nitro group. In DMF, JRV-7 and JRV-9 are equally most effective, which contain p-chloro and p-hydroxy groups respectively. The inhibition is more in DMSO than in DMF

Thus, both solvent and substitution plays an important role in inhibiting any strain.

Figure 4.10: Antibacterial activity of pyrazolines against Gram positive bacteria in [A] DMSO and [B] DMF.



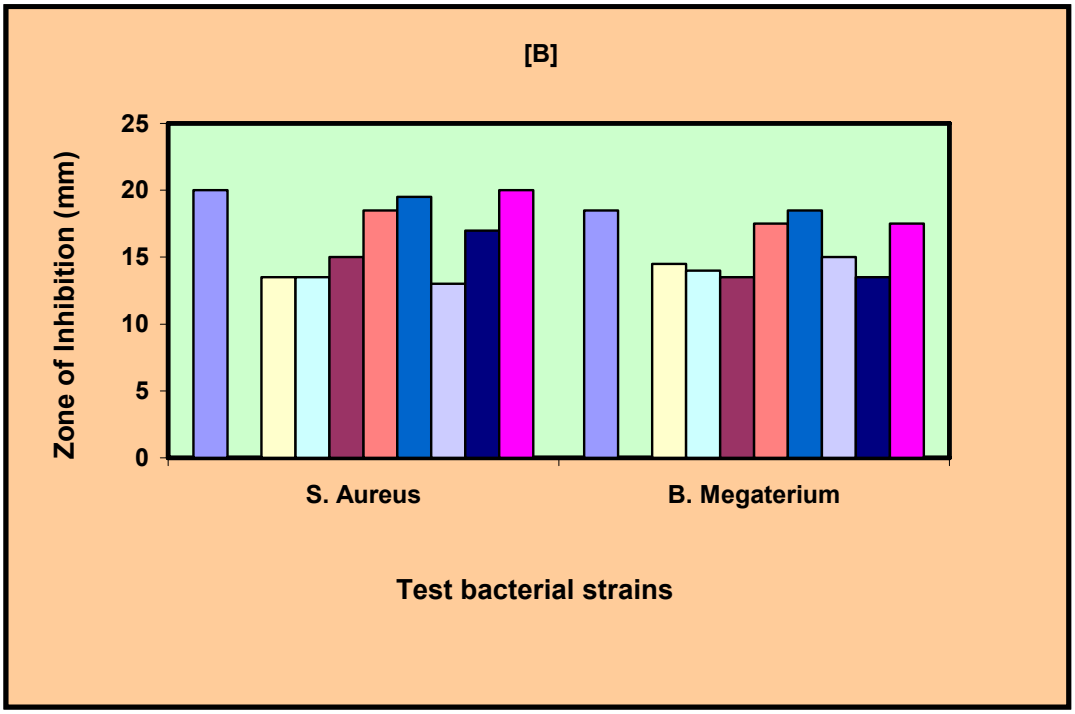


Figure 4.11: Antibacterial activity of pyrazolines against Gram negative bacteria in [A] DMSO and [B] DMF.

JRV-1, JRV -2, JRV -3, JRV -4, JRV -5, JRV -6, JRV -7, JRV -8, JRV -9, JRV -10

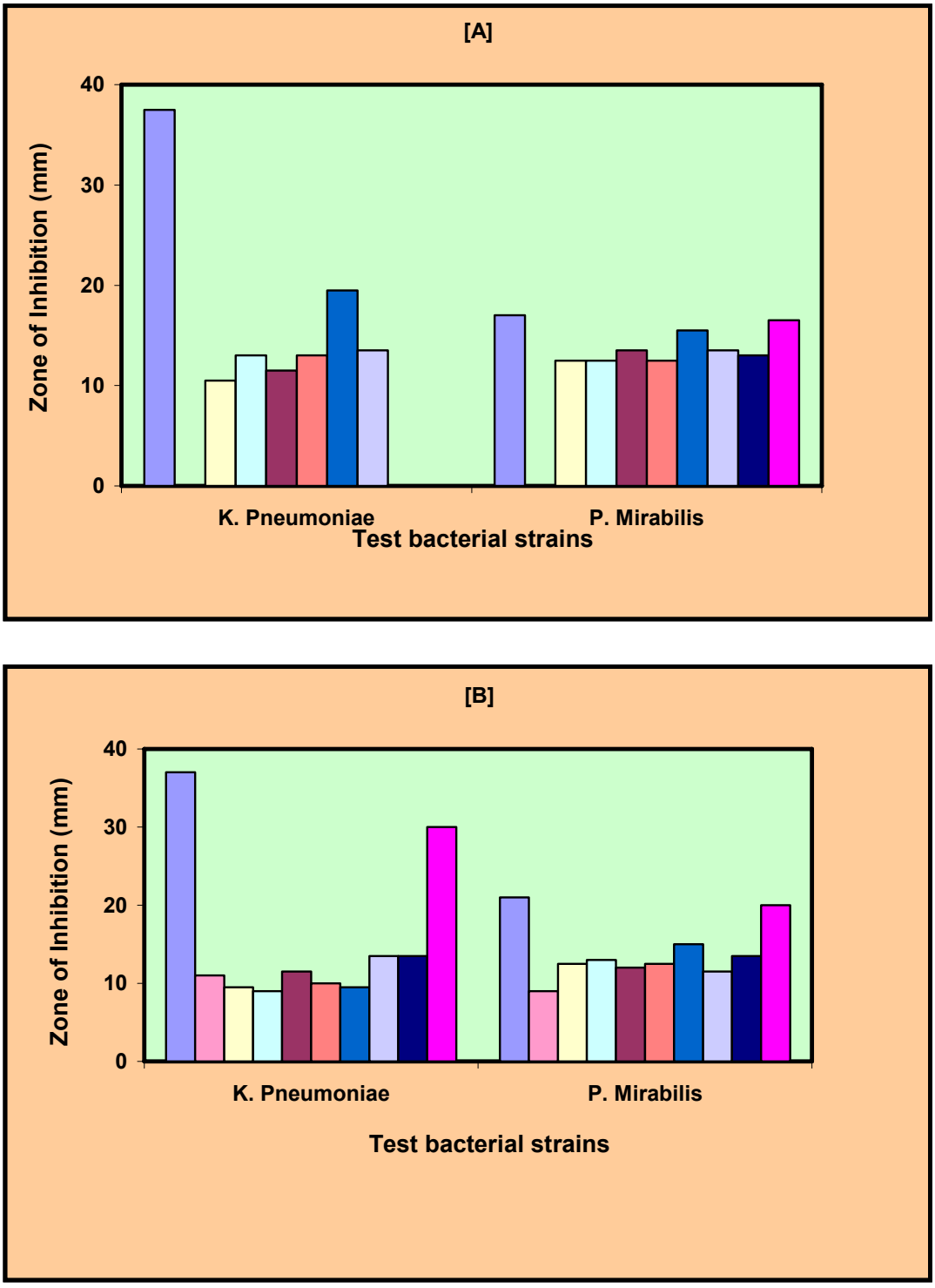
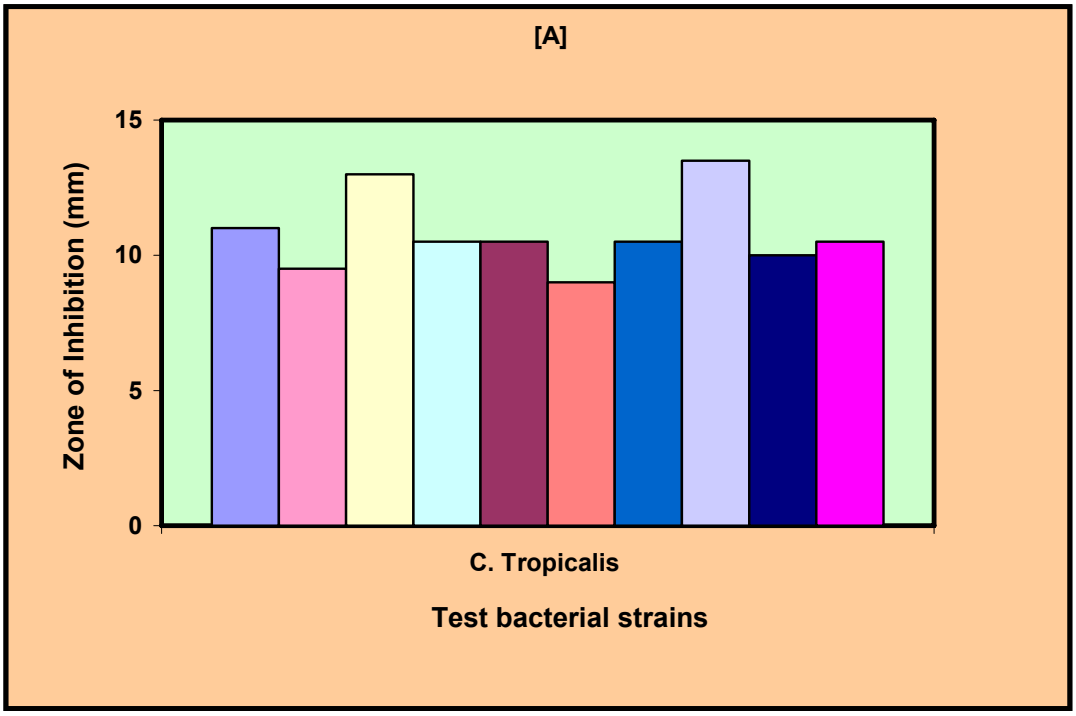
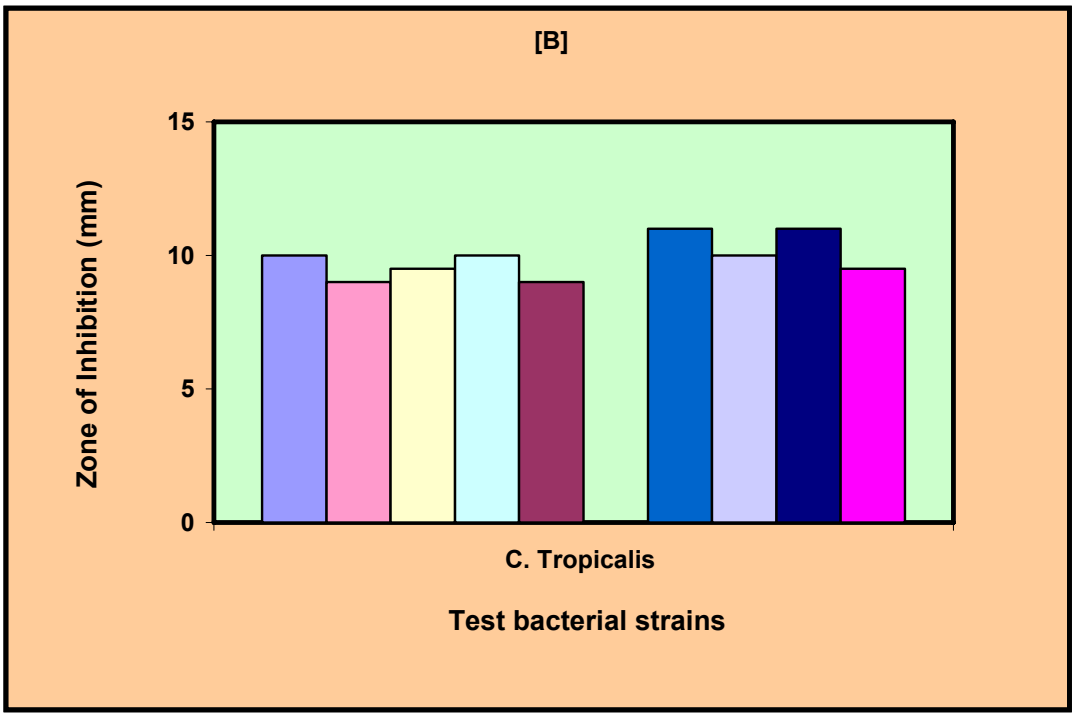


Figure 4.12: Antifungal activity of pyrazolines in [A] DMSO and [B] DMF.

JRV-1, JRV -2, JRV -3, JRV -4, JRV -5, JRV -6, JRV -7, JRV -8, JRV -9, JRV -10





Sulphonamides

For VSM series, the inhibition against Gram positive bacteria is shown in Figure 4.13 for both DMSO and DMF. It is observed that against both the

strains in both the solvents VSM-3 exhibited no inhibition. In DMSO, for *S. aureus*, VSM-7 showed maximum inhibition and VSM-10 showed minimum inhibition. VSM-3 and VSM-5 showed no inhibition at all. For *B. megaterium*, both VSM-7 and VSM-8 showed maximum inhibition whereas VSM-5 exhibited minimum inhibition. Thus, in DMSO, VSM-7 is the most effective compound for the studied bacteria. It contains chloro group at 6^{th} position and carboxylic group at 3^{rd} position.

In DMF also, VSM-7 exhibited maximum inhibition for both the studied Gram positive bacteria.

The inhibition depends on the solvent, substitution of compound structure and bacterial strain. VSM-3, VSM-5, VSM-7 and VSM-10 contain 3-carboxilic-4-chloro, 3-carboxilic-4-methoxy, 3-carboxilic-6-chloro and p-acetamide as a substituent respectively.

Thus, the presence of 3-carboxilic-6-chloro increases the inhibition in the studied solvents against studied strains.

Figure 4.14 shows zone of inhibition against Gram negative bacteria in DMSO and DMF. Against *K. pneumoniae*, again the inhibition is maximum for VSM-7 and minimum for VSM-4 in DMSO. VSM-3 and VSM-5 showed no inhibition at all. For *P. mirabilis,* all the studied compounds are found to be effective in DMSO, among which VSM-8 showed maximum inhibition. Thus, for Gram negative bacteria, 3-carboxilic-6-chloro (in VSM-7) and 3-carboxilic-4-chloro (in VSM-8) are most effective in inhibiting *K. pneumoniae* and *P. mirabilis* respectively in DMSO.

In DMF, against *K. pneumoniae*, VSM-5 showed maximum activity, whereas VSM-1, VSM-2, VSM-3 and VSM-4 showed no inhibition at all. For *P. mirabilis,* VSM-2 showed maximum inhibition, whereas VSM-3 shows no inhibition at all. Thus, in DMF, 3-carboxilic-6-methoxy (in VSM-5) and 3-carboxilic-6-methyl (in VSM-2) are most effective in inhibiting *K. pneumoniae* and *P. mirabilis* respectively.

Comparison of inhibition in both the solvents shows that DMF is better solvent for the studied Gram negative bacteria.

Figure 4.15 shows the zone of inhibition against a fungal strain in DMSO and DMF. In both the solvents, all the studied compounds exhibited

inhibition against this fungal strain. However, inhibition is more in DMSO than in DMF.

In DMSO, VSM-1, VSM-2, VSM-5 and VSM-7 exhibited maximum inhibition whereas in DMF, VSM-2, VSM-7, VSM-8 and VSM-9 showed maximum inhibition.

Thus, it is concluded that most of the studied compounds are effective for this fungal strain *C. tropicalis* and DMSO is better solvent for this strain.

Figure 4.13: Antibacterial activity of sulphonamides against Gram positive bacteria in [A] DMSO and [B] DMF.

VSM-1, VSM-2, VSM -3, VSM-4, VSM -5, VSM-6, VSM -7, VSM-8, VSM -9, VSM -10

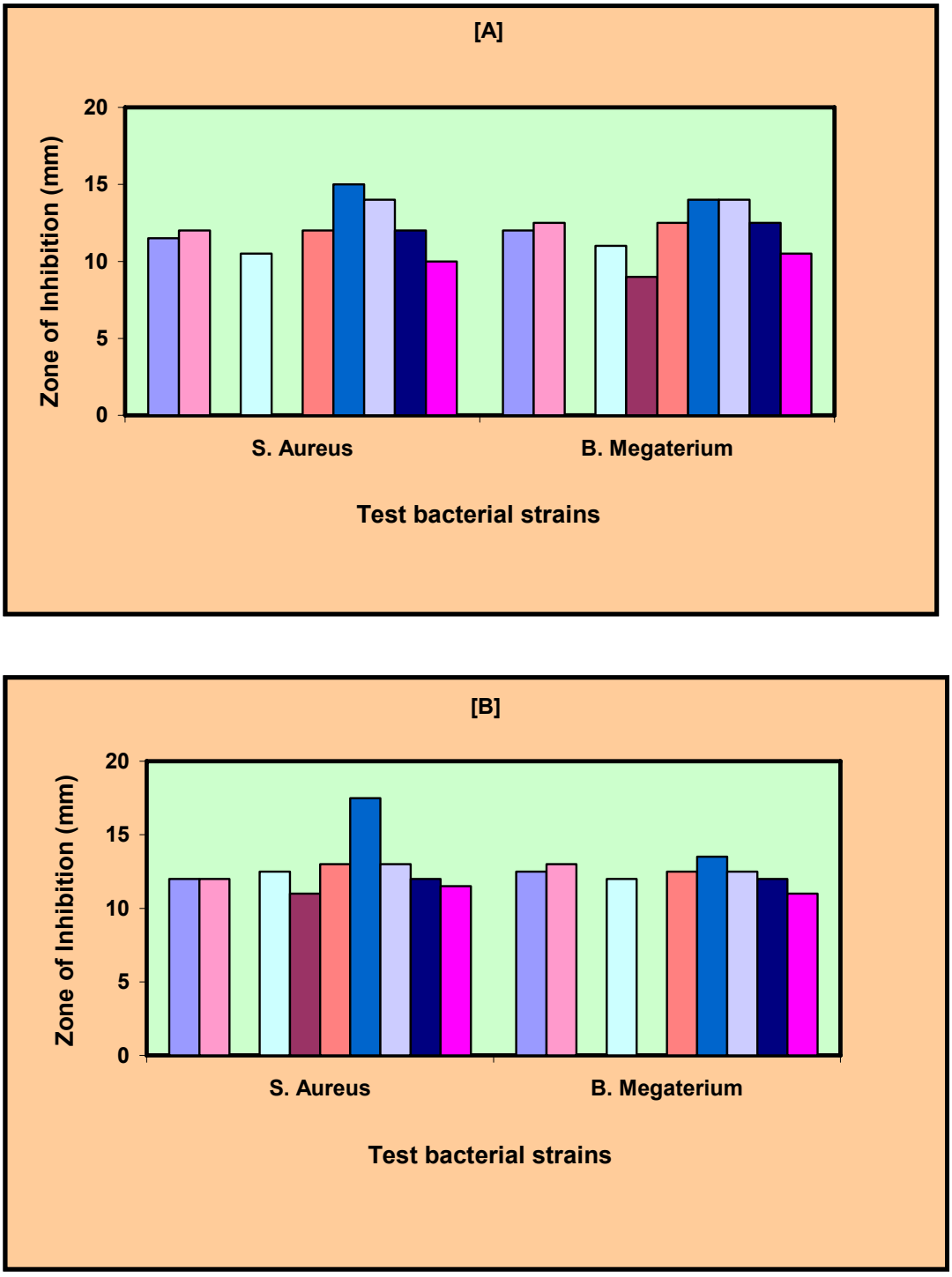


Figure 4.14: Antibacterial activity of sulphonamides against Gram negative bacteria in [A] DMSO and [B] DMF.

VSM-1, VSM-2, VSM -3, VSM-4, VSM -5, VSM-6, VSM -7, VSM-8, VSM -9, VSM -10

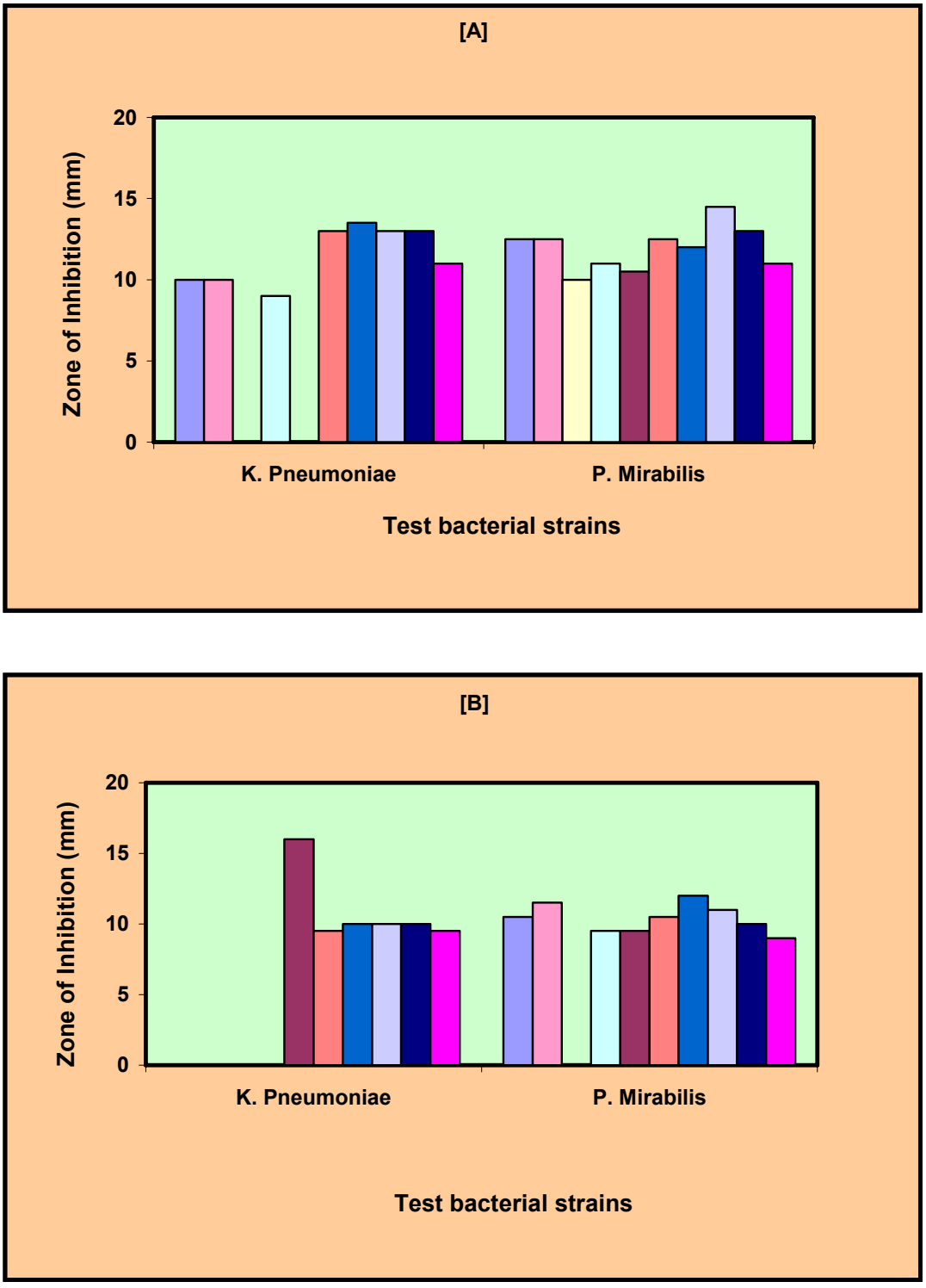
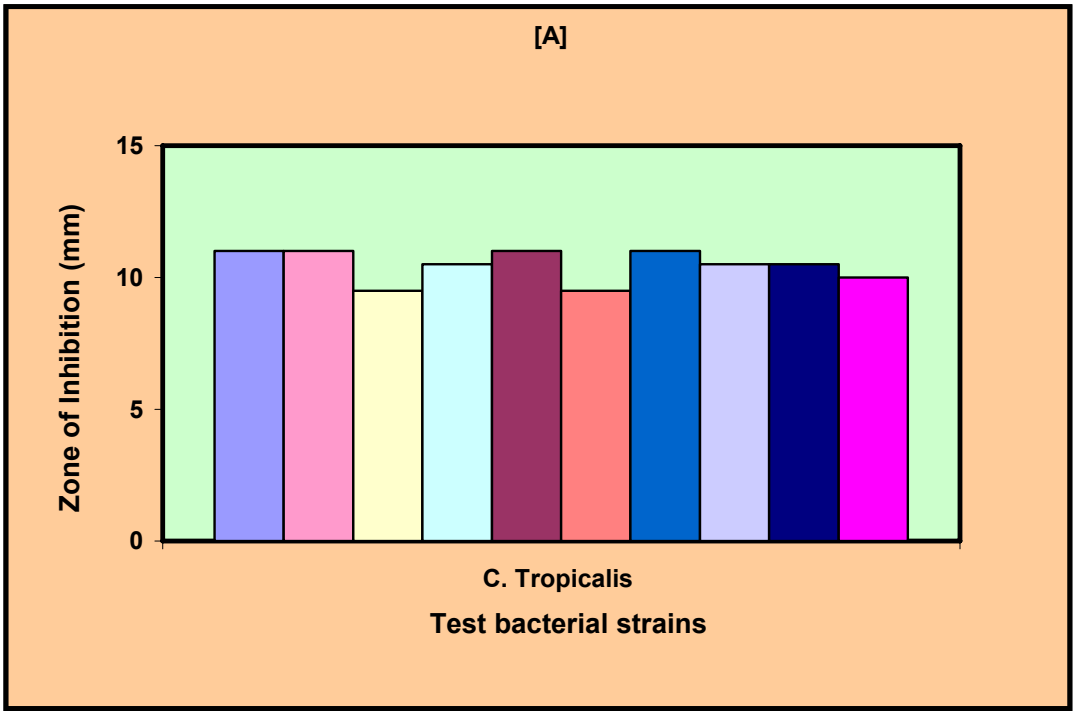
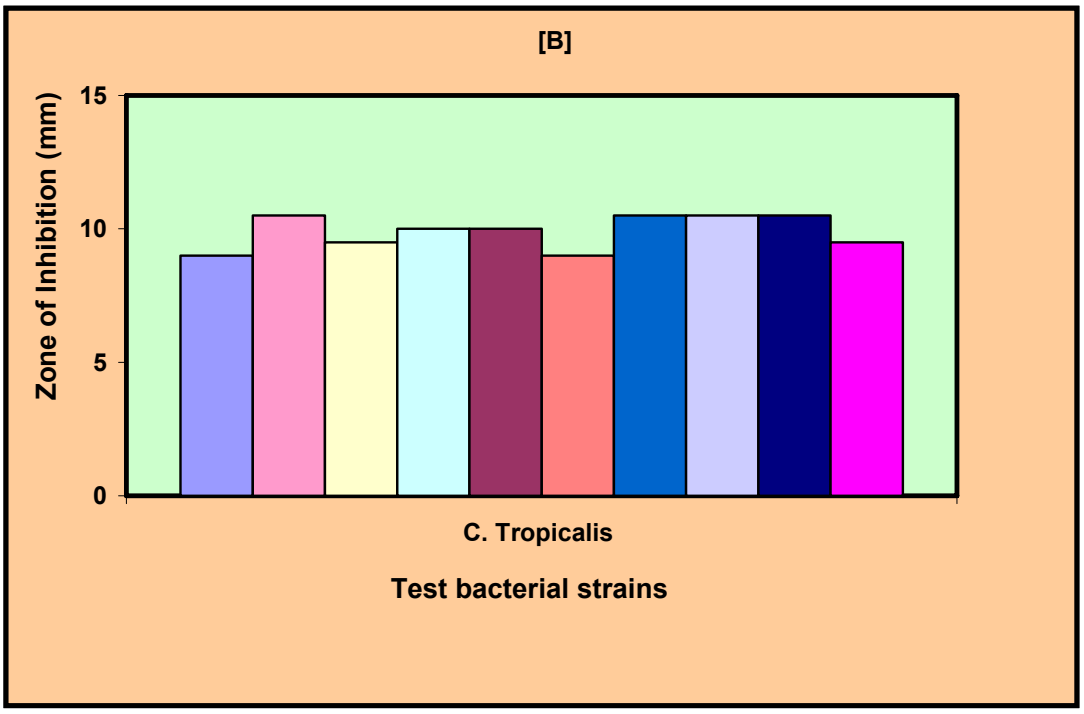


Figure 4.15: Antifungal activity of sulphonamides in [A] DMSO and [B] DMF.

JRM-1, JRM -2, JRM -3, JRM -4, JRM -5, JRM -6, JRM -7, JRM -8, JRM -9, JRM -10





REFERENCES

[1] K. Hugo; "QSAR and 3D QSAR in drug design Part-2 applications and problems" *Drug Design,* ***2(12),*** *538 (1997).*

[2] Cheg, D.; "Relationship of quantitative structure and pharmacokinetics in fluoroquinolone antibacterials", *World J Gastroenterol,* ***13(17)****, 2496, (2007)*

[3] T. Langer and S. Bryant; "3D Quantitative structure–property relationships" The *Practice of Med. Chem.,* ***3,*** *587-604 (2008),*

[4] V. Shelyakin, V. Dyachenko and A. Sharanin; "4-Methyl-3- cyanopyridine -2(1H)-thione." *Khimiya Geterots. Soedinenii,* ***(2)****, 269 (1995).*

[5] V. Naik and H. Naik; "Synthesis of some new pyrazoline derivatives and related compounds from chalcones and their antibacterial activity." Asian J. Chem., ***11(4)***, 1522-24 (1999).

[6] K. Mogilaiah and G. Sudhakar; "Synthesis of pyrazoline, pyrimidine and 1, 5 - benzodiazepine derivatives of 1, 8-naphthyridine and evaluation of antibacterial activity." *Ind. J. Chem.,* ***42B(3)****, 636-40 (2003).*

[7] S. Huang, R. Li, P. Connolly, G. Xu, M. Gaul, S. Emanuel, R. Kenneth and M. Lee; "Synthesis and biological study of 4- aminopyrimidine -5-carboxaldehyde oximes as antiproliferative VEGFR-2 inhibitors." *Bioorg. Med. Chem. Let.,* ***16(23),*** *6063-66 (2006).*

[8] I. Kamil and K, Ozdemir; "Antimicrobial activity screening of some sulfonamide derivatives on some Nocardia species and isolates." *Microbio. Res.,* ***164(1)****, 49-58 (2009).*

[9] J. A. Riddick, W. Bunger and T. Sakano; Organic Solvents-Physical Properties and methods of purification, Fourth Edition., Techniques of Chemistry, **II**, A Wiley-Interscience Publication, John Wiley, New York (1986).

[10] C. Perez, M. Paul and P. Bazerque; *Acta Biol. Med. Exp.* ***15****, 113 (1990).*

[11] J. Parekh, P. Inamdhar, R. Nair, S. Baluja and S. Chanda; "Synthesis and antibacterial activity of some Schiff bases derived from 4-aminobenzoic acid", *J. Serb. Chem. Soc.* ***70****, 1155 (2005).*

A COMPREHENSIVE SUMMARY OF THE WORK

The present work is divided into the following chapters:

CHAPTER - 1: This chapter describes the importance of heterocyclic compounds with aims and objective of the present work.

CHAPTER - 2:

Part-1 deals with the synthesis of cyanopyridines, aminopyri -midines, 1,5-benzodiazepines, pyrazolines and sulphonamides bearing quinoline moiety are described along with their physical constant data. The characterizations of synthesized compounds were done by IR, NMR and mass spectral data. The spectra and the characteristic peak positions of IR and NMR spectra of some compounds are reported. Further, mass spectra and possible fragmentation schemes are given in this chapter.

Part-2 deals with the comparison of synthesis of pyrazolines by conventional thermal heating, microwave assisted and ultrasound irradiation methods. It is observed that both microwave and ultrasound methods give comparatively good % yield of products than conventional method. Further, by using these techniques, reaction time is reduced to few minutes in microwave and to few hours in ultrasound technique.

CHAPTER - 3: The physicochemical properties of synthesized cyanopyridines were also studied at 298.15 K. The different properties are given in different sections. For the study of all physicochemical properties, DMF and DMSO were used as a solvent.

Section-I: This section describes the acoustical studied of cyanopyridines in DMF and DMSO solutions at 298.15 K over a wide range of concentrations. For this, density, viscosity and ultrasonic velocity of solutions were measured. From these experimental data, various acoustical parameters have been evaluated which helped to understand the different types of interactions occurring in the solutions. It is observed that for all the studied compounds in both the solvents, solute-solvent interactions dominate.

Section-II: In this section, the refractive index and densities of cyanopyridines were measured in DMF and DMSO solutions at 298.15 K. The density of solid compounds was evaluated from the experimental density values of solutions. Further, theoretical values of densities were evaluated and were compared with those calculated experimentally. The values are found to be different, which may be due to solvation of ions in solutions. In solutions of different solvents, density is found to be different due to different interactions. The molar refraction and refractive index of compounds are also found to be different in each solvent.

Section-III: This section deals with the conductance of studied compounds in solutions of various concentrations in DMF and DMSO at 298.15 K. It is observed that for all the studied compounds, conductivities are less in DMSO than in DMF. Further, all the studied compounds are weak electrolytes in the studied solvents.

Section-IV: This section describes the heat of solution of all the studied compounds in DMF and DMSO at different temperatures (308.15 -328.15 K). It is observed that the solubility of all the compounds increases linearly with temperature in both the solvents. Comparison of solubility of these compounds in DMF and DMSO shows that overall solubility is greater in DMSO than in DMF.

Further, some thermodynamic parameters such as enthalpy (ΔH_{sol}), Gibb's energy (,ΔG_{sol}) and entropy (ΔS_{sol}) have been calculated from the solubility data. All ΔH_{sol} ,ΔG_{sol} and ΔS_{sol} values are found to be positive. The positive ΔH_{sol} indicates endothermic dissolution of compounds whereas positive ΔG_{sol} suggests that the dissolution process is not spontaneous. The positive entropy is due to randomness in dissolution process.

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Section-V: This section describes partition coefficient of snthesised cyanopyridines in n-octanol-water system by UV speectroscopy at different pH. Out of 10 studied compounds, CP-10 exhibits maximum hydrophobic nature.

Section-VI: The thermal properties of synthesized cyanopyridines are described in this section. DSC and TGA thermo grams were scanned at the heating rate of 10^0 C per minute. It is observed that thermal stability depends on the presence of substituents in the compound. From all the studied compounds, CP-7 is most unstable whereas CP-9 is most stable. The stability of the compound depends on the substituent group. The presence of hydroxyl group (as in CP-9) increased the stability whereas chloro group at para position decreased the stability (as in CP-7).

Further, the melting points determined by DSC and by open capillary methods are found to be in good agreement.

Section-VII: In this section, the dissociation constants of cyanopyridines in DMF: water systems (90:10) are studied. It is observed that acidity is minimum in CP-04 having amino group as expected whereas for CP-07 having chloro group, acidity is maximum.

CHAPTER - 4: The antibacterial activities of all the synthesized compounds in DMF and DMSO, which screened against Gram positive and Gram negative bacteria and fungal, are explained in this chapter. Different bacterial strains behave differently in different solvents. Further, the presence of different substituents also affects inhibition.

LIST OF PUBLISHED PAPERS

1. "Thermal studies of some azomethines of sulphonamide and race-acetophenone" Shipra Baluja and **Jagdish Movaliya;** J. of Ultra Chem., **3(2),** 216-220 (2007).
2. "Acoustical studies of some derivatives of 4-amino benzoic acid in 1, 4-dioxane and dimethyl formamide at 308.15 K" Shipra Baluja; Nayan Vekariya and **Jagdish Movaliya**; Iran. J. Chem. Chem. Eng. **27(1)**, 129-135 (2008).
3. "Physicochemical studies of some azomethines of p-amino benzoic acid in solutions 1, 4 dioxane and DMF at 308.15 K" Shipra Baluja, Pranav Inamdar and **Jagdish Movaliya;** The ICFAI Uni. J. Chem., **2(2)**, 22-30 (2009)
4. "Thermal profile and decomposition kinetics of some new schiff bases derived from 4-amino antipyrine" Shipra Baluja, **Jagdish Movaliya** and Nilesh Godvani, Int. J. Appl. Chem. (Accepted)
5. "Acoustical studies of some derivatives of 1,5-benzodiazepines Formamide and Tetrahydrofuran Solutions at 298.15" S. Baluja, **J. Movaliya** and N. Godvani, Russ. J. Phy. Chem. A, **83(13)**, 2223-29 (2009)
6. "Synthesis and thermal analysis of some 1, 2, 4-triazole derivatives" Shipra Baluja, Nikunj Kachhadia, **Jagdish Movaliya** and Asif Solanki; Int. J. Chem. Sci., 7(2), 976-980 (2009)
7. "Antibacterial studies of some metal complexes of coumarin chalcones" Shipra Baluja, **Jagdish Movaliya** and Rahul Bhalodia, J. Inst. Chem., 81, 102-109 (2009).
8. "Excess thermodynamic properties of binary mixtures of acetaphenone with methanol, hexane, DMF and THF at 308.15 K" S. Baluja, **J. Movaliya** and N. Godvani, Int. J. Pure Appl. Phys., (Accepted)