

## LIST OF PUBLICATIONS

1. **Joseph V. A.**, J. H. Pandya, V. K. Gupta and R. N. Jadeja, "Synthesis, structural characterization, spectroscopic studies and antimicrobial activities of Schiff base ligands and their metal complexes derived from 2-hydroxy-3-methoxybenzaldehyde", *Journal of the Indian Chemical Society*, 89(11) (2012) 1455-1464.
2. **Joseph V. A.**, Komal M. Vyas, Jignesh H. Pandya, Vivek K. Gupta and R.N. Jadeja, "Studies on DNA binding behavior of biologically active Cu(II) complexes of Schiff bases containing acyl pyrazolones and 2-ethanolamine", *Journal of Coordination Chemistry*, 66( 6) (2013) 1094–1106.
3. **Joseph V. A.**, J. H. Pandya and R. N. Jadeja, "Spectral studies, crystal structure and biological evaluation of O-vanillin–4-aminoantipyrine Schiff base and its metal complexes", *Journal of The Maharaja Sayajirao University of Baroda*, 49(1) (2014) 29-44.
4. **V.A. Joseph**, J.H. Pandya and R.N. Jadeja, "Syntheses, crystal structure and biological evaluation of Schiff bases and copper complexes derived from 4-formylpyrazolone" *Journal of Molecular Structure*, 1081 (2015) 443–448.
5. **Joseph VA**, George JJ, Pandya JH and Jadeja RN, "O-Vanillin and Some of its Novel Schiff Bases: A Cheminformatic Approach to Identify their Biological Functions", *Theoretical & Computational Science*, 2 (2015): 136. doi:10.4172/jtco.1000136

## NATIONAL/ INTERNATIONAL CONFERENCES

1. Poster Presented in the 'National conference on chemical sciences in new millennium' held on 8th January 2012 at Pacific University, Udaipur.
2. Poster presented in the Regional Science Congress, 2012 held at the Department of Chemistry, The M. S. University of Baroda, Vadodara on September 15-16, 2012.
3. Poster Presented in the 20<sup>th</sup> ISCB International Conference, Department of Chemistry, University of Delhi held on 1<sup>st</sup>-4<sup>th</sup> March 2014.

## Synthesis, structural characterization, spectroscopic studies and antimicrobial activities of Schiff base ligands and their metal complexes derived from 2-hydroxy-3-methoxybenzaldehyde

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Manuscript received online 05 February 2012, revised 17 February 2012, accepted 20 February 2012

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**Abstract :** We depict the synthesis of two new Schiff base ligands, formed by the condensation of 2-hydroxy-3-methoxybenzaldehyde with 2-amino-5-methylpyridine or 2-amino-5-bromopyridine. All of these ligands have been characterized on the basis of elemental analysis, IR, <sup>1</sup>H NMR and Mass spectral data. The molecular geometry of 2-(5-methylpyridin-2-ylimino)methyl)-6-methoxyphenol has been determined by single crystal X-ray study. It reveals that this ligand exist in phenol-imine tautomeric form in the solid state. The reaction of these ligands with Cu<sup>II</sup> and Ni<sup>II</sup> resulted in the formation of mononuclear complexes having the general composition [ML<sub>1</sub>·NO<sub>3</sub>]<sub>2</sub>·H<sub>2</sub>O. These complexes have been characterized on the basis of elemental analysis, metal-estimation, molar conductivity, IR, UV-Visible, ESI-Mass, thermal analysis and magnetic measurements. Non-electrolytic behavior of complexes indicates the absence of counter ion. The studies indicate a square planar geometry of the metal complexes. The Schiff base ligands and their metal complexes have been tested for antimicrobial activity against Gram-positive bacteria; *Staphylococcus aureus* and *Bacillus subtilis* and Gram-negative bacteria; *Escherichia coli* and *Pseudomonas aeruginosa*.

**Keywords :** Schiff base metal complexes, crystal structure, antimicrobial activity.

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### Introduction

Schiff bases have been widely used as ligands in the formation of transition metal complexes. Although many structures of transition metal complexes with Schiff base ligands have been determined, a relatively small number of free Schiff bases have been structurally characterized<sup>1-6</sup>. However, knowing the structures of free Schiff base ligands could be important in view of comparison with the structure of Schiff base complexes. The Schiff bases are very important tools for the inorganic chemists as these are widely used to design molecular ferromagnets, in catalysis, in biological modeling applications, as liquid crystals and as heterogeneous catalysts<sup>7-9</sup>. Schiff base ligands containing various donor atoms (like N, O, S, etc.) show broad biological activity and are of special interest because of the variety of ways in which they are bonded to the transition metal ions<sup>10,11</sup>. The Schiff bases of salicylaldehyde and aminopyridines have been characterized in

detail in solid state and in solution<sup>12,13</sup> and proposed as highly sensitive spectrometric and spectrofluorimetric reagents for Cu<sup>II</sup><sup>14,15</sup>. However, analogous heteroaromatic Schiff bases derived from 2-hydroxy-3-methoxybenzaldehyde (*o*-vanillin) have not been investigated so thoroughly. The mono and bis-Schiff bases of *o*-vanillin and 2,3-diaminopyridine have been used as ionophores in a Cu<sup>II</sup> selective electrochemical sensor<sup>16</sup>. These compounds as well as their metal complexes have been found to possess biological activity<sup>17</sup>. Antibacterial activity has also been reported for the ruthenium(II) complex of the Schiff base of *o*-vanillin and 2-aminopyridine<sup>18</sup>.

### Results and discussion

All the ligands and their complexes are air and moisture free crystalline solids. The metal complexes are intensely colored. The metal complexes are insoluble in common organic solvents and only soluble in DMF and

## Studies on DNA binding behavior of biologically active Cu(II) complexes of Schiff bases containing acyl pyrazolones and 2-ethanolamine

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(Received 14 April 2012; in final form 13 November 2012)

Pyrazolone derivatives (*Z*)-4-((2-hydroxyethylimino)(*p*-tolyl)methyl)-3-methyl-1-phenyl-1*H*-pyrazol-5(4*H*)-one [PMP-EA] (**1**), (*Z*)-1-(3-chlorophenyl)-4-((2-hydroxyethylimino)(*p*-tolyl)methyl)-3-methyl-1*H*-pyrazol-5(4*H*)-one [MCPMP-EA] (**2**), and (*Z*)-4-((2-hydroxyethylimino)(*p*-tolyl)methyl)-3-methyl-1-*p*-tolyl-1*H*-pyrazol-5(4*H*)-one [PTPMP-EA] (**3**) have been synthesized and characterized. The molecular geometry of **2** has been determined by single-crystal X-ray study. These ligands exist in amine-one tautomeric form in the solid state. Three copper(II) complexes, [Cu(PMP-EA)(H<sub>2</sub>O)<sub>2</sub>] (**4**), [Cu(MCPMP-EA)(H<sub>2</sub>O)<sub>2</sub>] (**5**), and [Cu(PTPMP-EA)(H<sub>2</sub>O)<sub>2</sub>] (**6**), respectively, have been synthesized using these ligands and characterized by microanalytical data, molar conductivity, IR, UV–Visible, FAB–Mass, magnetic measurement, TG–DTA studies, and ESR spectral studies; Cu(II) is five-coordinated with [ML(H<sub>2</sub>O)<sub>2</sub>] composition. The interaction of the complexes with CT-DNA (calfthymus) was investigated using different methods. The results suggest that the copper complexes bind to DNA *via* intercalation and can quench the fluorescence intensity of EB bound to DNA.

**Keywords:** Schiff bases; Crystal structure; Cu(II) complexes; DNA binding

### 1. Introduction

Pyrazolone-5 derivatives form an important class of compounds important in medicinal chemistry for their high biological activity [1, 2]. Even the simplest pyrazolone-5 derivatives are well-known analgesics, widely used in medicine. 4-Acyl pyrazolone derivatives have many potential dimmers with diverse coordination, capable of chelating and bridging properties [3].

Schiff bases of acyl pyrazolones are ligands for many metal ions, promoted by high sensitivity with a series of ions. Schiff bases have diverse biological, pharmacological, antitumor activity and exceptional chelating ability [4–6].

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# Spectral studies, crystal structure and biological evaluation of O-vanillin–4-aminoantipyrine Schiff base and its metal complexes

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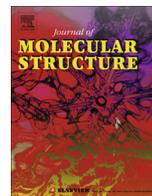
## Abstract:

In the present study a new series of Cu(II), Ni(II) and V(IV) complexes of Schiff base ligand 4-(2-hydroxy-3-methoxybenzylideneamino)-1,2-dihydro-2,3-dimethyl-1-phenylpyrazol-5-one have been prepared. The Schiff base ligand V-4AAP has been characterized on the basis of IR, <sup>1</sup>H NMR and Mass spectroscopy. The molecular geometry of ligand also has been determined by single crystal X-ray study. It reveals that the ligand exist in phenol-imine tautomeric form in the solid state. The metal complexes have been characterized on the basis of elemental analysis, metal-estimation, molar conductivity, IR, UV-Visible, ESI-Mass and thermal analysis. Non-electrolytic behavior of complexes indicates the absence of counter ion. The studies indicate square planar geometry for Copper and Nickel complexes and tetragonal pyramidal for Oxovanadium complex. The Schiff base ligand and its metal complexes have been tested for antimicrobial activity against Gram-positive bacteria; *Staphylococcus aureus* and *Bacillus subtilis* and Gram-negative bacteria; *Escherichia coli* and *Pseudomonas aeruginosa*.

**Key words:** O-vanilline-4-aminoantipyrine, Schiff base metal complexes, Crystal structure

## 1. Introduction:

Schiff base complexes are considered to be among the most important stereochemical models in main group and transition metal coordination chemistry due to their



# Syntheses, crystal structure and biological evaluation of Schiff bases and copper complexes derived from 4-formylpyrazolone



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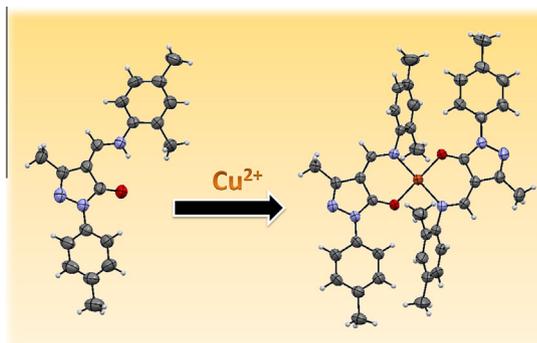
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## HIGHLIGHTS

- Two new Cu(II) complexes were synthesized and characterized.
- Single-crystal XRD of the Schiff base ligand shows it exists in amine-one form.
- Single-crystal XRD analysis of both the complexes was carried out.
- The Cu(II) complexes exist in square planer geometry.
- Antibacterial activities of Cu(II) complexes were carried out.

## GRAPHICAL ABSTRACT

Two new Cu(II) complexes of pyrazolone based Schiff ligands were synthesized and found to exist in square planer geometry.



## ARTICLE INFO

### Article history:

Received 1 August 2014

Received in revised form 16 September 2014

Accepted 22 October 2014

Available online 28 October 2014

### Keywords:

Schiff base

Copper(II)

Pyrazolone

Crystal structure

Antimicrobial activity

## ABSTRACT

Two new pyrazolone based Schiff base ligands 4-((2,4-dimethylphenylimino)methyl)-4,5-dihydro-3-methyl-1-p-tolyl-1H-pyrazol-5-ol [PTPMP-ME] and 4-((3,4-difluorophenylimino)methyl)-4,5-dihydro-3-methyl-1-p-tolyl-1H-pyrazol-5-ol [PTPMP-F] were synthesized. Using these Schiff base ligands two new Copper(II) complexes, [Cu(PTPMP-ME)<sub>2</sub>] (1) and [Cu(PTPMP-F)<sub>2</sub>] (2) were synthesized. The ligands and their copper complexes were characterized by IR, <sup>1</sup>H NMR, mass, UV–Visible spectroscopy, molar conductivity and magnetic measurement. The molecular geometry of Schiff base ligand PTPMP-ME and copper complexes were determined by single-crystal X-ray analysis. On the basis of single crystal X-ray analysis and spectroscopic techniques, square planar geometry of the complexes was proposed. The Schiff base ligands and their metal complexes were tested for antimicrobial activity against Gram-positive bacteria; *Staphylococcus aureus* and *Bacillus subtilis* and Gram-negative bacteria; *Escherichia coli* and *Pseudomonas aeruginosa*.

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## Introduction

Pyrazolone, as a prominent structural motif, is found in numerous active compounds. Pyrazolone derivatives have occupied a unique position in drug discovery due to their broad range of biological activities, such as anti-inflammatory, antibacterial, antiviral

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## O-Vanillin and Some of its Novel Schiff Bases: A Cheminformatic Approach to Identify their Biological Functions

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### Abstract

Ortho-Vanillin (2-Hydroxy-3-methoxybenzaldehyde) is an organic solid present in the extracts and essential oils of many plants. Its functional groups include aldehyde, ether and phenol. Recent years, most ortho-vanillin is used in the study of mutagenesis and as a synthetic precursor for pharmaceuticals. The current study is focused on the prediction of biological target through target fishing approach for the novel o- vanillin and some of their Schiff bases which are synthesized by our group. Various tools and databases were employed to identify the biological function of the synthesized O-vanillin derivatives, the obtained results were confirmed through docking and molecular dynamics simulation studies.

**Keywords:** O-Vanillin; Schiff bases; Cheminformatic; Molecular dynamics

### Introduction

A huge amount of protein sequences and chemical structure data has been generated from sequencing centres and synthetic chemistry laboratories as a result of the fast development in Bioinformatics and Cheminformatics. This interdisciplinary approach saved both time and money in identifying novel drug molecules for the known protein and nucleic acid targets through high throughput and virtual screening of chemical compounds. The problem of having huge number of chemical molecules with unknown biological functions was solved after 1990 when many chemical-diversity-related approaches like structural descriptor computations, structural similarity algorithms, diversified compound selections, classification algorithms and library enumerations were developed. To compliment this many filtering techniques to discriminate toxic and non-toxic compounds were also discovered alongside the Cheminformatics timeline [1-4].

The current medicinal chemistry research draws heavily from polypharmacology which is a multi-target approach wherein single chemical molecule interact with multiple targets instead of a single one. For example, many of the most effective drugs currently in use such as Gleevec (anti-cancer drug), psychiatry drugs - serotonin reuptake inhibitors - and aspirin (anti-inflammatory drug) act upon multiple targets rather than a one to one mechanism [5-8].

Computational target fishing is a novel approach which predicts the biological function of small molecules by identifying their interacting proteins. It involves various cheminformatics tools, databases, and machine learning algorithms [9-11]. Many previous studies evidenced the prediction of multi-target small molecules [12] through target fishing approach [13-15]. The current study is focused on the prediction of biological target through target fishing approach for the novel o- vanillin and some of its novel Schiff bases which are synthesized by our group [16-18]. The obtained results were confirmed via docking studies.

### Materials and Methods

The synthesised seven O-vanillin chemical molecules were used to carry out this Cheminformatics study. The list of molecules with two dimensional structures are shown in Figure 1.

### Ligand preparation

It involves the addition of hydrogens, 2D to 3D conversion, bond lengths and bond angles fixation, energy minimisation with correct chiralities, ionization states, tautomers, stereochemistries and ring conformations. All Molecules were prepared by using LigPrep module of Schrodinger [19].

### Drug likeliness property prediction

QikProp module of Schrodinger is used to predict drug likeliness of prepared molecules. It predicts widest variety of relevant properties such as LogP, MDCK, HERG, Lipinski's rule of 5 and many others [20]. The QikProp screened molecules were exported and taken for further analysis.

### Toxicity prediction

ToxPredict tool was used to predict the toxicity level of molecules obtained from the previous stage. It predicts and reports on toxicities including several parameters such as carcinogenicity, mutagenicity, human toxicological hazards and other 20 parameters [21]. Toxicity is the adverse effect of a chemical compound on the biological functions.

### Biological function prediction

A diverse range of publicly available Bioinformatics and Cheminformatics tools and databases were used to identify protein targets and biological activity of screened molecules from previous steps. Due to limitation in the accuracy of each tool, various tools were employed to get more accurate results.

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**Received** November 09, 2015; **Accepted** November 27, 2015; **Published** December 08, 2015

**Citation:** Joseph VA, George JJ, Pandya JH, Jadeja RN (2015) O-Vanillin and Some of its Novel Schiff Bases: A Cheminformatic Approach to Identify their Biological Functions. J Theor Comput Sci 2: 136. doi:[10.4172/jtco.1000136](https://doi.org/10.4172/jtco.1000136)

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