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Title of the collaborative activity: Research Collaboration

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Synthesis of Some Novel 5-(8-Substituted-11*H*-Indolo[3,2-c]Isoquinolin-5-ylthio)-1′,3′,4′-Oxadiazol-2-Amines Bearing Thiazolidinones and Azetidinones as Potential Antimicrobial, Antioxidant, Antituberculosis, and Anticancer Agents

Vaijinath A. Verma[a] and Anand R. Saundane[b]

[a]Department of Chemistry, S. S. Margol College of Arts, Science and Commerce, Shahabad, Kalaburagi, Karnataka, India; [b]Department of Post-Graduate Studies and Research in Chemistry, Gulbarga University, Kalaburagi, Karnataka, India

ABSTRACT

As a part of systematic investigation, a novel series of 5-(8-Substituted-11*H*-Indolo[3,2-c] isoquinolin-5-ylthio)-*N*-{(5-substituted-2-phenyl-1*H*-indol-3-yl)methylene)-1′,3′,4′-oxadiazol-2-amine analogs were synthesized and appraised for their *in vitro* antimicrobial, antioxidant, anti-tuberculosis and anticancer activity against three tumor cell lines. Amidst the compounds tested **6a** has demonstrated intense antibacterial and radical scavenging activities. Compound **7a** revealed efficient to fantabulous antifungal activity. It is worth noting that compound **6g** was most active antituberculosis agent against H37Rv strain *Mycobacterium tuberculosis*. In case of anticancer activity compounds **6e** and **8e** against all the three tumor cell lines manifested remarkable cytotoxic activity. Ferrous ions (Fe^{3+}) reducing antioxidant power was shown by compound **6e**.

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KEYWORDS
Azetidinone; indolo[3,2-c]isoquinoline; oxadiazole; thiazolidinone

Introduction

Tuberculosis (TB) and cancer are serious, extensive talked in to clinical medicine and still no universal adequate medications handling them have been synthesized. TB is an infection with *Mycobacterium tuberculosis* (MTB) and extends significant morbidity and mortality worldwide.[1] This study expect importance to TB which has turned out to be a standout amongst the most common sicknesses that is in charge of death of around one billion people during the last two centuries.[2] TB endures an intolerable general health in India, accounting for one-third of the global burden and it has been estimated that 3.5 million of the population are infected with TB.[2,3] The World Health Organization approximates that 8 million people attribute new infection with TB apiece year.[4,5] TB is one of the major causes of death amongst infectious diseases. Mycobacterial cell wall components may induce nitric oxide production and reactive oxygen species (ROS), both concerned in carcinogenesis.[6] A survey conducted by the National Cancer Institute found that patients with pulmonary TB had enhanced risk of lung cancer and estimated a twofold elevation in risk of lung cancer in men with TB.[1,7] In addition, Cancer is fatal disease with intensifying reasons for death and statistics report that an expected 20 million people worldwide cases per year by 2020.[8] The main effectuate of cancer is because of the spectacular free

CONTACT Vaijinath A. Verma drvermachem@gmail.com Department of Chemistry, S. S. Margol College of Arts, Science and Commerce, Shahabad-585 228, Kalaburagi, Karnataka, India.

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Synthesis of Schiff Base Indolyl-1,3,4-Oxadiazole, Thiazolidinone and Azetidinone as Efficient Antimicrobial, Antioxidant, Antituberculosis and Anticancer Agents

Vaijinath A. Verma[1,*], Anand R. Saundane[2] and Rajkumar S. Meti[3]

[1]Department of Chemistry, S.S. Margol College of Arts, Science and Commerce, Shahabad-585228, India

[2]Department of Post-Graduate Studies and Research in Chemistry, Gulbarga University, Kalaburagi- 585106, India

[3]Department of Biochemistry, Mangalore University, P.G. Centre Chikka Aluvara, Kodagu-571232, India

*To whom correspondence to be addressed: Fax: +91 8474 204472 Tel: +91 8474 204473 E-mail: drvermachem@gmail.com

Abstract

The present investigation was under-taken to synthesize the Schiff base indole derivatives bearing of 1,3,4-oxadiazole thiazolidinone and azetidinone moieties. New series of 5-(5-substituted-3-phenyl- 1*H*-indol-2-yl)-*N*-[(5-substituted-2-phenyl-1*H*-indol-3-yl)methylene]-1,3,4-oxadiazol-2-amines and screened their biological activities. Compound **4a** showed excellent antibacterial and radical scavenging activities. Compound **5a** revealed efficient to antifungal activity. In addition, compound **4a** was found to be most active against H37Rv strain *Mycobacterium tuberculosis*. In case of anticancer activity methoxy compounds **4e** and 6e against all the three tumor cell lines manifested remarkable cytotoxic activity. Compounds **4e**, **5e** and **6e** have shown strong ferrous ions (Fe^{3+}) reducing antioxidant power (FRAP) among the compounds screened. Compound **5b** showed more potent of metal chelating on Fe^{2+} ions activity at all concentrations.

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Keywords

Indole, Oxadiazole, Azetidinone, Thiazolidinone, Microbial activities

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Synthesis of Cefixime Nanoparticles an Attempt to Enhance Their Development and Validation of Spectrophotometric Methods for the Determination of Pharmaceutical Forms

Basavaraj Hiremath[1]*, Nagesh Gunavanthrao Yernale[2,3] and B.H.M. Mruthyunjayaswamy[3]

[1]*Department of Chemistry, S. S. Margol Degree College, Shahabad – 585 228, Dist. Kalaburagi Karnataka, India*
[2]*Department of Chemistry, Guru Nanak First Grade Science, Commerce and Post Graduate College, Bidar – 585 403, Karnataka, India*
[3]*Department of Post Graduate Studies and Research in Chemistry, Gulbarga University, Kalaburagi – 585 106, Karnataka, India*

**Corresponding author :Basavaraj Hiremath, Department of Chemistry, S. S. Margol Degree College, Shahabad – 585 228, Dist. Kalaburagi Karnataka, India, E-mail: drbhiremath25@gmail.com*

ABSTRACT

Cefixime nanoparticles were prepared by anti-solvent precipitation with syringe pump (APSP) method. Two simple and sensitive spectrophotometric methods I and II for the analysis of cefixime nanoparticles in either pure form or their pharmaceutical formulations are described. Method I is based on the oxidation of the drug with ferric ion succeed by complex development reaction with 1, 10-phenanthroline (1, 10-PTL) to obtain orange-red colored chromogen shows λ_{max} at 510 nm also the method II on the reaction between diazotized drug with diphenylamine (DPA) in neutral medium to yield a pink-colored product which has λ_{max} at 512 nm. The products are unchanging for more than 10 and 4 hrs respectively. Common excipients used as additives in pharmaceutical dosage do not impede the proposed methods. Thus the proposed methods proved to be easy, low cost, and accurate, are highly reproducible and have been applied to a broad range of pharmaceutical preparations and the outcome compares favorably with those of the official method. Prepared nanoparticles samples showed a better outcome than bulk drug samples.

Keywords: Cefixime; Nanoparticles; 1, 10-PTL; DPA; Dizotization; Spectrophotometry.

INTRODUCTION

Cefixime is designated chemically as (Z)-7-[2-(2-Aminothiazol-4-yl)-2-(carboxymethoxyimino) acetamido]-3-cephem-4-carboxylic acidtrihydrate [1,2]. Cefexime is an antibiotic, and a 3rd generation cephalosporin is extremely steady in the presence of beta-lactamase enzymes [3]. Cefexime is used in the treatment of the subsequent infections stimulated by vulnerable strains of the selected microorganism; uncomplicated urinary tract infectivity caused by *Escherichia coli* and *Proteus mirabilis*, otitis media caused by *Haemophilus influenza* (beta-lactamase positive and negative strains), *Moraxella catrrhails* mainly of which are beta-lactamase positive, and *S. pyogenes*, pharyngitis and tonsillitis induced by *S. pyogenes*, acute bronchitis, acute exacerbations of chronic bronchitis induced by *Streptococcus pneumonia* and *Haemophilusinfluenzae* and uncomplicated gonorrhea caused by *Neisseria gonorrhea* [4]. Cefixime was used as a model drug [5] and it has a broad antibacterial spectrum against various Gram-positive and Gram-negative bacteria, including Haemophilusinfluenzae, Neisseria gonorrhoeae, Escherichia coli, and Klebsiellapneumoniae resistant to ampicillin, cephalexin, cefaclor, and trimethoprimsulfamethoxazole. It is used for the treatment of susceptible infections, including gonorrhea, otitis media, pharyngitis, lower respiratory-tract infections such as bronchitis, and urinary-tract infections [6-8].

Literature survey reveals that very few methods like spectrophotometric [9-11], high-performance liquid chromatography (HPLC) [12-14], high-performance thin-layer chromatography (HPTLC) [15-17], LC-MS [18,19], high-performance capillary electrophoresis [20,21] and spectrofluorimetric methods [22-24] are available for the analysis of cefexime. Various most recent drugs are of slight water solubility and little dissolution rates [25]. Their solubility and dissolution rapidity can be rising by reducing particle size [26,27]. Reducing the size of the particles will increase surface area, which can raise the speed of dissolution in aqueous resembling body fluids [28-30]. The dissolution speed is straightway proportional to the exposed surface area to the medium used in dissolution [31]. The small size of nanoparticles means that they contain disparate physico-chemical and physiological properties relate to outsized particles, such as condensed light scattering, enhanced stability to gravitational separation and aggregation, quicker dispersion rates, elevated solubility, and higher diffusion rates due to biological barriers [32].

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Research Paper

An Experimental Design Approach for Validation and Optimisation of Spectrophotometric Determination of Cefixime in Pharmaceutical Dosage Form

H. BASAVARAJ* AND B. H. M. MRUTHYUNJAYASWAMY[1]

Department of Chemistry, Shri Prabhu and J. M. Bhora Degree College, Shorapur, Karnataka 585224, [1]Department of Chemistry, Gulbarga University, Kalaburagi, Karnataka 585106, India

Two simple, sensitive and precise spectrophotometric methods for the assay of cefixime in either pure form or in its pharmaceutical dosage form are described. The method I is based on the reaction of salicylaldehyde with cefixime resulting in a yellow coloured product, absorbs at λ_{max} 425 nm. The second method describes the reaction between the diazotized drug and N-(1-naphthyl)ethylenediamine dihydrochloride to yield a purple coloured product with λ_{max} at 567 nm. The reaction conditions were optimized to get maximum colour intensity. The absorbance was found to extend linearly with increasing the concentration of cefixime the systems obeyed the Beer's law within the range of 2-10 µg/ml and 5-25 µg/ml for salicylaldehyde and N-(1-naphthyl)ethylenediamine dihydrochloride methods. Common excipients used as additives in pharmaceutical dosage don't interfere within the proposed analytical methods. The products are stable for over 6 h and 10 h respectively. The proposed methods are simple, sensitive, accurate and suitable for quality control uses.

Key words: Cefixime, salicylaldehyde, N-(1-naphthyl)ethylenediamine dihydrochloride, pharmaceutical dosage form, validation

Cefixime (CFX) is designated and chemically known as 7-(Z)-[2-(2-aminothiazol-4-yl)-2-carboxymethoxyimino)acetamido]-3-cephem-4-carboxylic acid trihydrate[1,2]. CFX is an antibiotic and third generation cephalosporin and it is extremely stable within the presence of beta-lactamase enzymes. CFX is employed within the treatment of the subsequent infections caused by susceptible strains of the designated microorganism; uncomplicated urinary tract infections caused by *Escherichia coli* and *Proteus mirabilis*, otitis media caused by *Haemophilus influenza* (beta-lactamase positive and negative strains), *Moraxella catarrhalis* most of which are beta-lactamase positive and *Streptococcus pyogenes*, pharyngitis and tonsillitis caused by *Streptococcus pyogenes*, acute bronchitis and acute exacerbations of continual bronchitis caused by *Streptococcus pneumonia* and *Haemophilus influenzae* and uncomplicated gonorrhea caused by *Neisseria gonorrhea*.

Literature survey reveals that only a few methods like spectrophotometric[3-6], High Performance Liquid Chromatography (HPLC)[7-10], High Performance Thin Layer Chromatography (HPTLC)[11,12], Liquid Chromatography-Mass Spectrometry (LC-MS)[13,14], high performance capillary electrophoresis[15,16] and spectrofluorimetric methods[17-19], are available for the analysis of CFX. In continuation of our research on spectrophotometric determination of organic compounds of pharmaceutical importance, this communication reports two spectrophotometric methods for the determination of CFX in either pure form or in pharmaceutical dosage forms. Both regents are used for the primary time in CFX analysis.

The simplicity of these methods is that the reagent utilized in both the methods is well available and therefore the chemistry of the reagent is already well established. The reaction involved these reagents are easy, rapid and

*Address for correspondence
E-mail: drbhiremath25@gmail.com

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