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A NOVEL USE OF OXIDATIVE COUPLING REACTIONS FOR DETERMINATION OF ANTIBIOTIC AND ANTI-INFLAMMATORY DRUGS IN PHARMACEUTICAL FORMULATIONS

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ABSTRACT

The present work describes new spectrophotometric methods for the assay of four drugs namely Meropenem (MPN), Cefditoren Pivoxil (CTP), Mesalamine (MSL) and Cefdinir (CDN) in both pure form and Pharmaceutical formulations. All methods involve the oxidative coupling reaction of MPN, CTP, MSL and CDN with 3-methyl-2-benzothiazolinone hydrazone hydrochloride (MBTH) in presence of Fe(III) in an acidic medium to form colored products with absorption maxima at 620, 630, 500 and 620 nm respectively. Beer's law was obeyed in the ranges of 5-25, 5-40, 5-25 and 2-12 µg/ml for MPN-MBTH, CTP-MBTH, MSL-MBTH and CDN-MBTH respectively. Statistical treatment of the experimental results indicates that the methods are precise and accurate. The proposed methods have been applied to the determination of the active components in commercial formulations with no interference from excipients. A comparative study between the suggested procedures and reference procedure for these compounds in the commercial formulations showed no significant difference between two procedures.

Keywords:

Spectrophotometry,
Meropenem,
Cefditoren Pivoxil,
Mesalamine,
Cefdinir,
3- methyl-2-benzothiazolinone
hydrazone hydrochloride (MBTH)

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INTRODUCTION: The IUPAC chemical name of Meropenem is (4R, 5S, 6s) – 3- [(2S, 5S)-5- (Di methyl carbamoyl) pyrrolidin-2-yl] sulfanyl – 6 – (1-hydroxy ethyl)- 4- methyl- 7- oxo- 1- azabicyclo [3.2.0] hept -2 ene-2-carboxylic acid. Meropenem is a broad-spectrum carbapenem antibiotic. It is active against Gram-positive and Gram – negative bacteria, exerts its action by penetrating bacterial cells readily and interfering with the synthesis of vital cell wall components, which leads to cell death.

Cefditoren Pivoxil is chemically (6R) - 7- [[[2Z)- 2- (2-amino- 1, 3- thiazol- 4- yl)- 2-methoxyiminoacetyl] amino]- 3- [(Z)- 2- (4- methyl- 1, 3- thiazol- 5- yl) ethenyl]- 8- oxo- 5- thia- 1- azabicyclo [4.2.0] oct- 2- ene- 2- carboxylic acid. It is a third generation cephalosporin with antibacterial activity against gram-positive and gram-negative pathogens.

Mesalamine is chemically known as 5-amino- 2- hydroxy benzoic acid, is an anti-inflammatory drug used to treat inflammation of the digestive tract (crohn's disease) and mild to moderate ulcerative colitis. It is a bowel-specific amino salicylate drug that is metabolized in the gut and has its predominant actions there, thereby having fewer systemic side effects.

Cefdinir is chemically (6R, 7R) - 7- [[[2Z) - 2- (2- amino-1, 3- thiazol- 4- yl) - 2-hydroxy imino acetyl] amino] - 3- ethenyl- 8- oxo- 5- thia- 1- azabicyclo [4.2.0] oct- 2 - ene- 2- carboxylic acid. It is a semi-synthetic, broad-spectrum antibiotic in the third generation of the cephalosporin class, proven effective for common bacterial infections of the ear, sinus, throat and skin. Several methods¹⁻¹⁶ have been reported in the literature for analytical determination of these drugs. The literature survey on the analytical applications of 3-methyl-2-benzothiazolinone hydrazone hydrochloride (MBTH) indicates that it has not been earlier

reported as reagent for the spectrophotometric determination of these drugs in either biological fluids or pharmaceutical formulations. Hence the authors have made an attempt to develop simple and sensitive methods for the determination of the cited drugs in bulk and pharmaceutical formulations.

Experimental: The drugs used for present investigation were obtained in highly pure form (pharmaceutical grade) from the local pharmaceutical industries Hyderabad. Their pharmaceutical preparations were procured from different commercial sources. All other reagents were of analytical grade. Spectrophotometric measurements were carried out through a Techcomp UV-2301 model UV-Visible spectrophotometer with 1cm matched quartz cells.

Standard Drug Solution: Accurately weighed 100 mg of each drug was dissolved in 100 ml of solvent (methanol for Meropenem, Cefditoren Pivoxil, Mesalamine and dimethyl sulfoxide for Cefdinir) in a volumetric flask to give a concentration of 1 mg/ml. The final working standard concentrations were brought to 250 µg/ml (for Meropenem, Cefditoren Pivoxil and Mesalamine), and 100 µg/ml (for Cefdinir).

Reagents: Aqueous solution of MBTH (0.2% w/v) and ferric chloride (0.7% w/v) in 0.5 N hydrochloric acid were prepared for these investigations.

Assay Procedure: Aliquots of working standard drug solution containing 0.5-5ml (250µg/ml for Meropenem or Cefditoren Pivoxil or Mesalamine, 100µg/ml for Cefdinir) were transferred into a series of 25 ml standard flasks. To each flask 1.5 ml of MBTH, 2 ml of ferric chloride were added and kept for 10 min., with occasional stirring and the volume was made up to mark with distilled water. The absorbance of green colored chromogen was measured at 620, 630, 500 and 620 nm for MPN-

MBTH, CTP-MBTH, MSL-MBTH and CDN-MBTH respectively against the reagent blank. The amount of drug in the sample was computed from its calibration curve.

Preparation of Sample solution: Accurately weighed formulation (tablet or capsule or vial) powder equivalent to 100 mg of drug was transferred to a 100 ml volumetric flask containing 50 ml of solvent, sonicated for 10 min. and diluted to 100 ml with solvent, the resulting solution was filtered through a Whatmann filter paper. From this suitable dilutions were made to obtain the working concentrations. The assay of formulation was carried out according to the general procedure.

Results and Discussion: In the proposed methods MBTH was oxidized by ferric chloride in acidic

medium followed by its coupling with the drug to form green colored complex showing absorption maximum at 620, 630, 500 and 620 nm for MPN-MBTH, CTP-MBTH, MSL-MBTH and CDN-MBTH respectively. The optical characteristics such as Beer's law limits, Molar absorptivity, Sandell's sensitivity for these methods are presented in **Table 1**. Regression characteristics like slope, intercept, and correlation coefficient are also shown in the Table 1. Commercial formulations were successfully analyzed by the proposed methods and the values obtained are presented in **Table 2**. The accuracy of these methods was ascertained by performing recovery experiments, which are also shown in Table 2. Recovery experiments indicate the absence of interferences from the commonly encountered pharmaceutical additives and excipients.

TABLE 1: OPTICAL CHARACTERISTICS OF THE PROPOSED METHODS

Parameter	MPN-MBTH	CTP-MBTH	MSL-MBTH	CDN-MBTH
λ max	620	630	500	620
Beer's law limits ($\mu\text{g/ml}$)	5-25	5-40	5-25	2-12
Molar absorptivity ($\text{l mol}^{-1} \text{cm}^{-1}$)	1.1105×10^3	0.2091×10^4	0.5274×10^3	0.2993×10^4
Sandell's sensitivity ($\mu\text{g cm}^{-2}$)	0.3453	0.2969	0.2904	0.1321
Regression equation ($Y = mX + b$)				
Slope (m)	0.0225	0.0196	0.026	0.0936
Intercept (b)	0.1056	0.0123	0.0602	0.0752
Correlation coefficient	0.9998	0.9984	0.9993	0.9987
R.S.D. (%)*	0.3227	0.8192	0.8147	0.4959
% Range of error (confidence limits)				
0.05 level	± 0.4006	± 1.0170	± 1.0114	± 0.6169
0.01 level	± 0.6645	± 1.6867	± 1.6774	± 1.0231

* Mean of five determinations

TABLE 2: ASSAY AND RECOVERY OF SELECTED DRUGS IN PHARMACEUTICAL FORMULATIONS

Drug	Method	Formulation type	Labeled Amount mg/tablet or capsule or vial	Amount found*	Recovery%**
Meropenem	MPN-MBTH	Vial	500	499.78 ± 0.111	99.59 ± 0.533
Cefditoren Pivoxil	CTP-MBTH	Tablet	200	199.89 ± 0.085	99.90 ± 0.139
Mesalamine	MSL-MBTH	Tablet	400	399.95 ± 0.044	99.93 ± 0.040
Cefdinir	CDN-MBTH	Capsule	300	299.91 ± 0.105	98.81 ± 0.137

* Mean of five determinations; ** Mean of three determinations

CONCLUSION: It could be concluded that the developed methods are simple, sensitive, precise, accurate and can be satisfactorily applied to the analysis of Meropenem, Cefditoren Pivoxil, Mesalamine and Cefdinir in bulk and Pharmaceutical formulations in the quality control.

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