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New Spectrophotometric Determination of Oxalamine phosphate in Bulk and Pharmaceutical Dosage forms

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ABSTRACT

Rapid, accurate, precise and economical UV-Visible spectrophotometric methods were developed for the determination of Oxalamine phosphate (OMP) in bulk and pharmaceutical formulations. These methods (Method-A and Method-B) were based on the formation of colored complexes with Iron (III), *o*-Phenonthroline (M-A) and Cobalt thiocyanate (M-B). The absorbance concentration of plots were linear over the concentration range 10-60µg/ml (Method-A) and 4-24 µg/ml (Method-B) respectively for both methods with a minimum detection limit (LOD) of 2.059 µg/ml (Method-A) and 0.106 µg/ml (Method-B), limit of quantification (LOQ) of 6.240 µg/ml (Method-A) and 3.240 µg/ml (Method-B) respectively. The absorbance was measured at 482 and 620 nm with use of the cited reagents, respectively. The reactions were extremely rapid at room temperature and absorbance values remain unchanged up to 18hrs. Recoveries were 97.90-102.06%. Interferences of the other ingredients and excipients were not observed. The proposed methods are simple and sensitive and this is the first reported complexometric methods for the determination of Oxalamine phosphate (OMP) in commercial tablets.

Keywords: UV-Visible Spectrophotometry; Oxalamine phosphate; *o*-Phenonthroline; Cobalt thiocyanate

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INTRODUCTION

Oxalamine phosphate (OMP, Perebron) [1, 2] (Figure.1) is used in the treatment of respiratory tract diseases, accompanied by cough or not such as pharyngitis, laryngitis, tracheitis, bronchitis, bronchiectasis and partussis. Chemically it is N, N-diethyl-2-(3-phenyl-1, 2, 4-oxadiazol-5-yl)ethanamine; phosphoric acid. It is an Antitussive Agents which suppress cough. They act centrally on the medullary cough center.

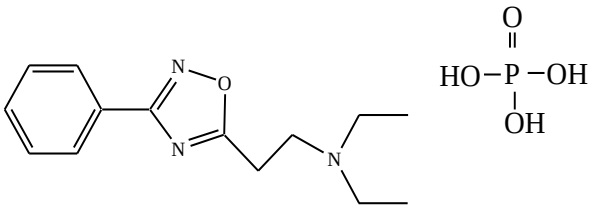


Figure.1.Structure of Oxalamine phosphate

Literature survey has been revealed that there are no UV-Visible spectrophotometric methods reported for the estimation of Oxalaminephosphate (OMP). Iron (III), *o*-Phenanthroline and Cobalt thiocyanate as compexing agents for the determination of many compounds of pharmaceutical interest is widely used. The complexes of Iron (III), *o*-Phenanthroline ions bear the advantage of being water soluble, and hence do not require any extraction procedure. But Cobalt thiocyanate is insoluble in water and hence requires extractive element i.e., nitrobenzene. Several compounds of pharmaceutical interest such as MoxifloxacinHcl[3], α-Tocopherol[4], Fluoroquinones[5], Etodolac[6], Pitavastatin[7], Disopyramide and Irbesartan[8], Anti-tissue and Anti Spasmodic drugs[9], Pipazethate Hcl[10], Methyl dopa[11], Anti emetic drugs[12,] Amoxylline, Ciprofloxacin and Piroxicam[13], and Cephalosporins[14] were determined.

In the current development the author proposed two UV-Visible spectrophotometric methods to determine the Oxalamine phosphate (OMP) in its bulk and pharmaceutical dosage forms are novel, economical, accurate and stable and these are mainly useful in pharmaceutical regular in house practices to reduce the cost.

MATERIALS AND METHOD

Apparatus

An ELICO-244, double beam UV-Visible spectrophotometer with 1cm quartz cells was used for all absorbance measurements under the following operating conditions. Scan speed medium (400nm/min), scan range 350-700nm with an ELICO-120 digital with glass pH electrode.

Chemicals and Reagents

All the reagents and solvents were of analytical grade and the pure drug was provided by

Arabindo laboratories Pvt. Ltd, Hyderabad. All reagents namely $FeCl_3$, *o*-Phenanthroline (*o*-PHEN), ortho phosphoric acid, cobalt thiocyanate (CTC) and nitrobenzene were supplied by Merk specialties pvt.Ltd; Mumbai and were used without any further purification. Double distilled water was used in the preparation of all the solutions. All the freshly prepared solutions were used. Commercial syrup form (Perebron) of Oxalamine phosphate was procured from local market.

a) $FeCl_3$solution (0.054%):- Prepared by dissolving 54 mg of anhydrous ferric chloride in 100 ml of distilled water.
b) *o*-Phenanthroline (0.2%):- Prepared by dissolving 200 mg of Phenanthroline in 100 ml of distilled water with warming.
c) Ortho phosphoric acid: - Prepared by diluting 1.27 ml of ortho phosphoric acid to 100 ml with distilled water. 10ml of this solution was diluted to 100ml with distilled water.
d) CTC solution: - Prepared by dissolving 7.25g of cobalt nitrate and 3.8g of ammonium thiocyanate in 100 ml distilled water.
e) Buffer solution (pH 2.0):- Prepared by mixing 3.6 ml of tri sodium citrate (0.1M) with 6.94 ml of HCl (0.1M) and pH was adjusted to 2.0
f) Nitrobenzene: - AR grade nitrobenzene was used.

Preparation of standard sample solutions

A stock solution was prepared by dissolving 100 mg of OMP in 100 ml distilled water from this working stranded solution equivalent to 200 µg/ml of OMP was obtained.

Preparation of test solution

From the Cough syrup formulation, Perebron (10mg/ml OMP), 1ml taken in 100 ml volumetric flask and volume was adjusted to mark with methanol. This working sample solution was having strength 100 µg/ml of OMP.

Methods for estimation of OMP

In this paper author has developed two methods for the determination of Oxalamine phosphate (OMP) in bulk and pharmaceutical formulations.

Method-A: Co-ordination complex formation of OMP with Fe (III) and *o* –PHEN

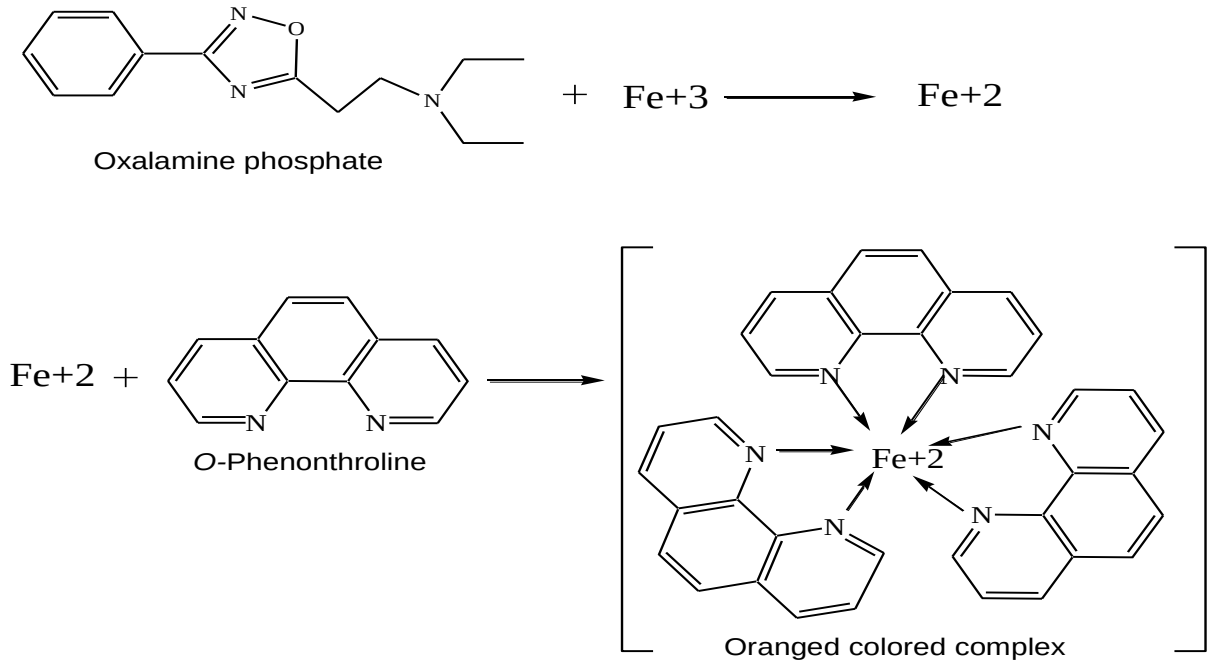
Method-B: Co-ordination complex formation of OMP with CTC

Scheme of the colored products

Method-A:

This method based on reduction of Fe^{+3} to Fe^{+2} of $FeCl_3$ with OMP and subsequent colored complex formation of the resulting Fe^{+2} ion with O-Phenanthroline and ortho phosphoric acid

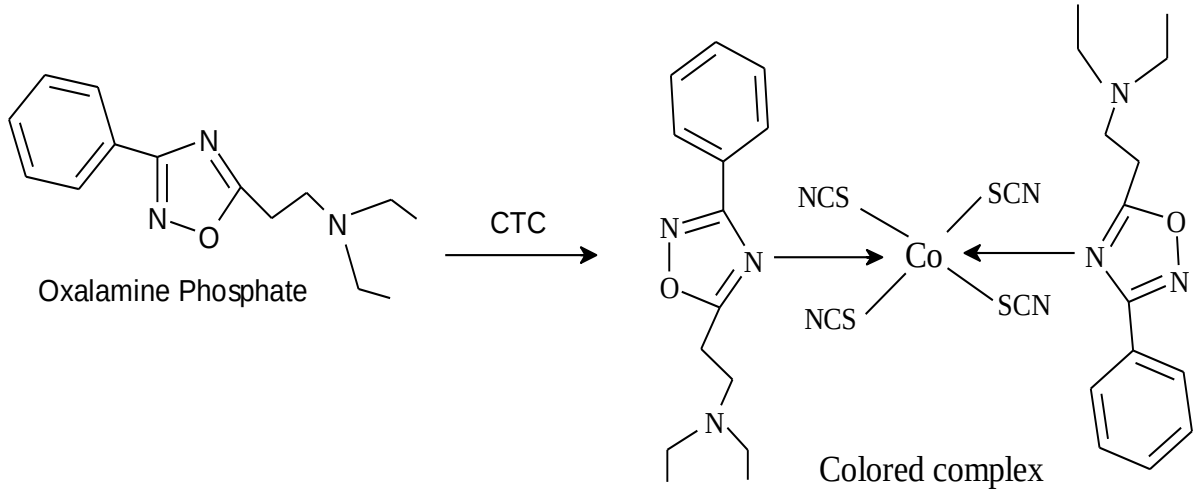
medium form an orange colored chromogen. **Scheme-I** represents the formation of colored species in the method[15].



Scheme-I

Method-B:

In this method the colored species formed is the co-ordination complex of drug (electron donor) and the central atom of CTC, which is extractible into nitrobenzene from aqueous solution. **Scheme –II** represents the formation of colored species in the method[16].



Scheme-II

Optimization of reaction conditions

The reactions were investigated on effect of the reaction time, the reaction temperature, buffer pH, choice of the organic solvent (nitrogen benzene) and ratio of the organic phase to the

aqueous phase, volume of *o*-PHEN as well as $FeCl_3$ and CTC solution. Control experiments were carried out by measuring absorbance at 482nm and 620nm of series of the solutions varying one and fixing the other parameter for Method-A and B respectively.

RESULTS AND DISUCCION

OMP was involved in co-ordination complex formation with Iron (III), *o*-Phenanthroline and Cobalt thiocyanate were quantitatively measured. The absorbance spectra of both methods (Method A & B) were drawn by plotting absorbance against wavelengths (Figure. 1 and 2) and the respective absorption spectra, the absorbance maximum were found to be at 482 and 620nm respectively. The amount of OMP was computed from the Beer-Lambert's plots (Figure.3) and (Figure.4) respectively.

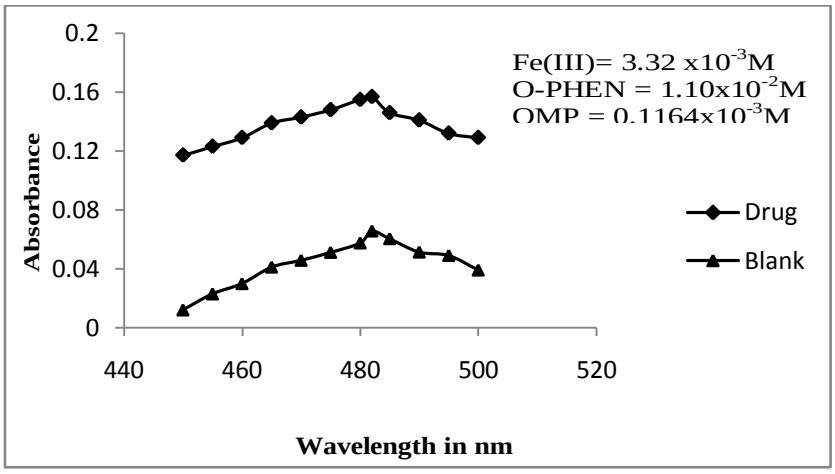


Figure.1. Absorbance spectrum of OMP with Fe III) +*o* –PHEN

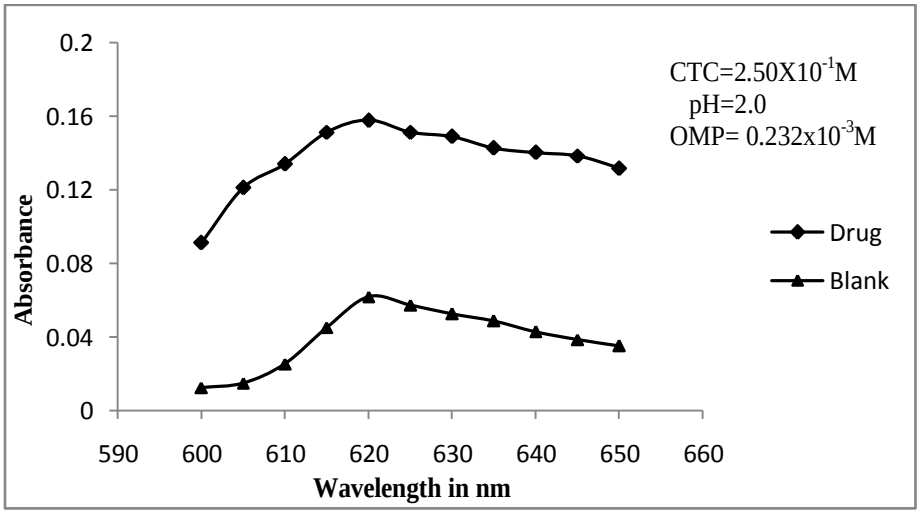


Figure .2. Absorbance spectrum of OMP with CTC

The calibration graphs (Figure.3&4) were linear over the concentration ranges within the permissible ranges. The optical characteristics and stastical data for the regression equation of

the proposed methods are presented in Table1. The amount of OMP was calculated from the Beer-Lambert's plots.

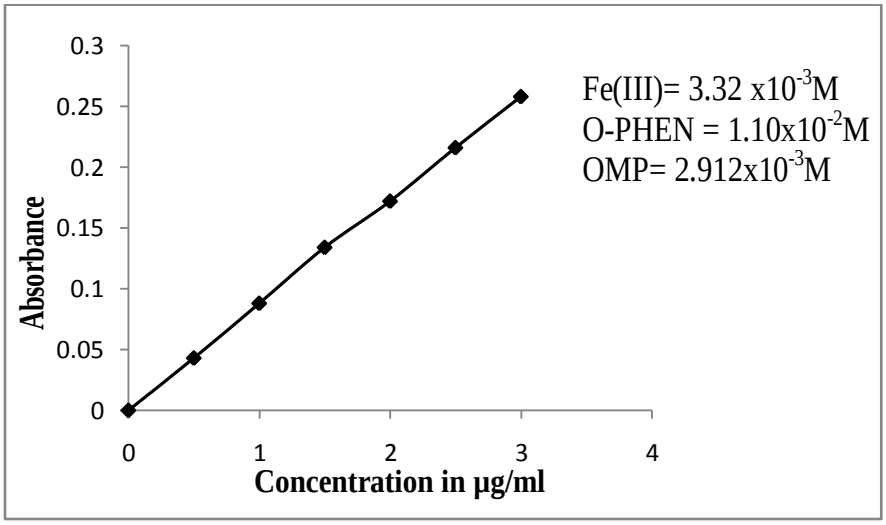


Figure.3. Beer's Lambert plot of OMP with Fe (III) +*o*-PHEN

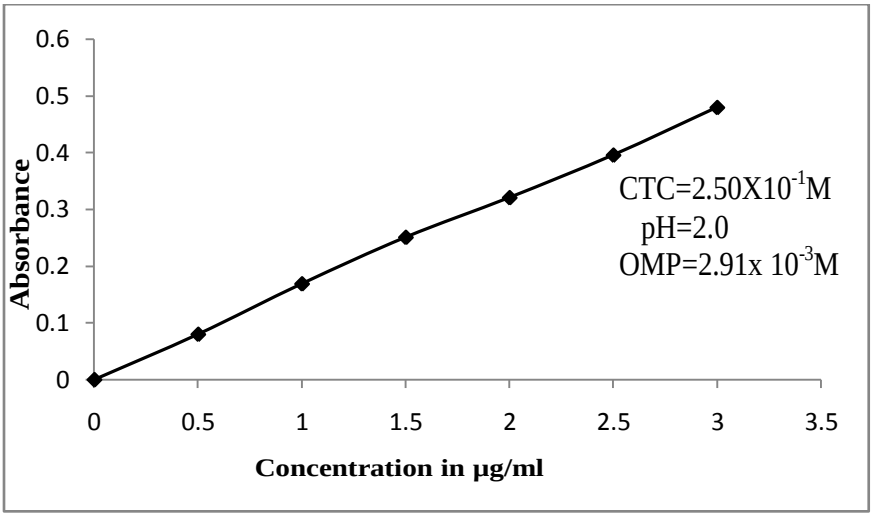


Figure.4. Beer's Lambert plot of OMP with CTC

Table 1: Optical characteristics, Precision and Accuracy of the proposed methods for OMP

Parameters	Method-A	Method-B
Maximum wave length λ_{max}	482	620
Beer's law Limits (µg/ml)	10.0-60.0	4-24
Optimum photometric Range µg/ml	12.08 – 58.01	03.06 – 21.02
Sandell's sensitivity (µg.cm^2/0.001absorbance limt)	0.1162	0.0591
Molar absorptivity lt/mole/cm	3.077x10^3	1.219x10^3
Standard Deviation (S_d)	0.00124	0.00129
Relative Standard Deviation (RSD)*	0.729	0.771
Slope (b)	0.001	0.004
Intercept (a)	0.086	0.158
Correlation coefficient (r)	0.9998	0.9999

% Range of error (Confidence limits)		
0.05 level	0.0010	0.6450
0.01 level	0.0015	0.9542
Limit of detection (LOD) µg/ml	2.0592	0.1069
Limit of quantification (LOQ) µg/ml	6.240	3.2401

*Average of six determinations considered

Optical characteristics

The optical characteristics such as Beer's law limits, Sandell's sensitivity, molar absorptivity, percent relative standard deviation, percent range of errors (0.05 and 0.01 confidence limits) were calculated for all the methods are summarized in Table-1. The values obtained for the determination of OMP in pharmaceutical dosage forms (syrup) by the proposed methods are presented in Table-2. Studies reveals that the common excipients and other additives usually present in the dosage forms not interfere in the proposed methods.

Precision and Accuracy

In order to test whether the colored products formed in these methods (Method A&B) adhere to Beer's law, the absorbances at maximum wavelength of series of six concentrations are plotted against concentration of the drug in µg/ml (Figure 3&4). Beer's law is obeyed within the limits of 10-60µg/ml (M-A) and 4-24 µg/ml (M-B) for both methods respectively. Molar absorptivity is found to be $3.077x10^3$ and $1.293x10^3$ for Method-A and Method-B respectively. Regression analysis of Beer's law plots at λ_{max} reveals a good correlation. The graphs shows negligible intercept and were described by regression equation, Y= bC + a (where Y is the absorbance of 1cm layer, b is the slope, a is the intercept and C is the concentration of the measured solution in µg/ml). The molar absorptivity of the resulting colored complexes indicates that the developed methods were high sensitivity.

Precision of the developed methods was ascertained from the absorbance values obtained by actual determination of six replicates of a fixed amount of the test solution. The optical characteristics; linear regression parameters, precision, and accuracy of the proposed methods are presented in Table-1. Pharmaceutical formulations containing OMP were successfully analyzed by the proposed methods. The results are presented in Table-2. When pharmaceutical preparations (syrup) containing OMP were analyzed, the results obtained by the proposed methods were compared with a reference method statically by means of t-test and F-test at 0.05 level of confidence limit and that are found to be good agreement with the labeled amount. The recovery with these methods was found to be 98-100%.

Table 2: Assay of OMP in pharmaceutical formulations

Method	Formulation	Labeled claim (mg)	**Found±SD (n=6)	% Recovery	RSD	*F-test	*t- test
Reference	Perebron	10	9.99±0.010	99.9	0.1020	……	…….
M-A	Perebron	10	9.99±0.014	99.9	0.1442	3.236	0.724
M-B	Perebron	10	9.98±0.017	99.8	0.1770	1.104	0.875

* Theoretical values at 0.05 level of confidence limit F=5.19, t=1.833.

** Mean of six determinations

CONCLUSION

The proposed methods are applicable for assay of OMP and have the advantage of a wider range. There was decreasing order of sensitivity for the methods $M_A > M_B$ and increasing order of λ_{max} among the proposed methods were $M_A < M_B$. As the formation of colored species both methods forms same complex with different reagents, The proposed methods were simple, selective, and reproducible and can be used in the routine analysis of oxalamine phosphate in bulk drug and pharmaceutical formulations with reasonable accuracy and precision.

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