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International Journal of ChemTech Research
CODEN(USA): IJCRGG ISSN : 0974-4290
Vol.2, No.3, pp 1838-1842, July-Sept 2010

New Spectrophotometric Methods for Estimation of Ethacridine Lactate in Pharmaceutical Formulations

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Abstract: Two simple and sensitive spectrophotometric methods (Method A and Method B) were developed for the estimation of Ethacridine lactate in pharmaceutical formulations. Method A is based on the oxidative coupling of Eathacridine Lactate with 3-methyl-2-benzothiazolinone hydrazone in the presence of Fe(III) to form a violet coloured chromoscme with a absorption maximum of 535nm. Method B is based on diazocoupling reaction with N-(1-napthyl) ethylenediamine dihydrochloride (B.M reagent) to form a stable purple coloured chromogen, which can be estimated at 540nm. Both the proposed methods (Method A and Method B) obey Beer's law in the concentration range of 2 to 8µg/ml. The methods were validated for use in routine quality control of Ethacridine lactate in pharmaceutical formulations.

Keywords: Ethacridine lactate, N-(1-napthyl)ethylenediamine dihydrochloride, 3-methyl-2-benzothiazolinone hydrazone and spectrophotometry.

Introduction :

Ethacridine lactate[1-6] is an antiseptic in solutions of 0.1%; it is also used as an agent for second trimester abortion. Upto 150ml of 0.1% solution is instilled extra amniotically using a foley catheter. Ethacredine as an abortificeant is found to be safer and better tolerated then 20% hypertonic saline. The chemical name of Ethacridine lactate is 2-ethoxy-6,9-diamino acridine monolactate monohydrate.it is official in BP,USP and EP. For the estimation of Ethacridine lactate few analytical methods by as HPLC [7-11] were reported. In the present investigation we developed two spectrophotometric methods based on Oxydative coupling reaction MBTH (Method A), diazotization followed by coupling with B.M reagent [12-19] (Method B).

Experimental Details

Instrumentation:

Systronics double beam UV/Visible spectrophotometer 2201 with matched quartz cells were used for the present investigation.

Reagents preparation:

1. 3-Methyl-2-benzothiazoloinone hydrazone*) solution (0.2 % w/v): prepared by dissolving 200 mg of* 3-Methyl-2-benzothiazoloinone hydrazone in 100 ml of distilled water.
2. *Ferric chloride solution (0.1% w/v):* prepared by dissolving 100 mg of Ferric chloride in 100ml of distilled water.
3. *Sodium nitrite solution (0.2% w/v):* 200 mg of sodium nitrite was dissolved in distilled water and made up to 100 ml.

4. *Hydrochloric acid (5N):* 425 ml of conc. HCl was taken and diluted to 1000 ml with distilled water.
5. *Ammonium sulphamate solution (0.5 %w/v):* 500 mg of ammonium sulphamate was dissolved in distilled water and made up to 100 ml.
6. *N-(1-napthyl) ethylenediamine dihydrochloride solution (0.1 % w/v):* 100 mg of N-(1-napthyl) ethylenediamine dihydrochloride was dissolved in 100 ml of distilled water.

Standard preparation:

About 100 mg of Ethacridine was accurately weighed and dissolved in 100 ml of water to get 1000 µg/ml stock solutions. This stock solution was further diluted with the same solvent to get working standard solution of 100 µg/ml.

Sample preparation:

The content of five vials was taken and mixed thoroughly. From this an accurately measured portion of the liquid content equivalent to 50 mg of the drug was dissolved in 70 ml of water and filtered. The filtrate was diluted to 100 ml with methanol. Later this solution was further diluted to get absorbance values within the calibration curve range.

Procedure for estimation:

Method A:

Aliquots of solution (100µg/ml) ranging from 0.2 to 0.8ml were transferred into a series of 10 ml volumetric flasks. To each flask 1.5 ml of Ferric choride solution and 1.5 ml of 3-methyl-2-benzothiazolinone hydrazone solution were added.and allowed to stand at room tempetature for 15 min.The final volume was adjusted to 10 ml with water and the absorbance of violet coloured species was measured at 535 nm against reagent blank. The amount of Ethacridine lactate was computed from calibration curve.

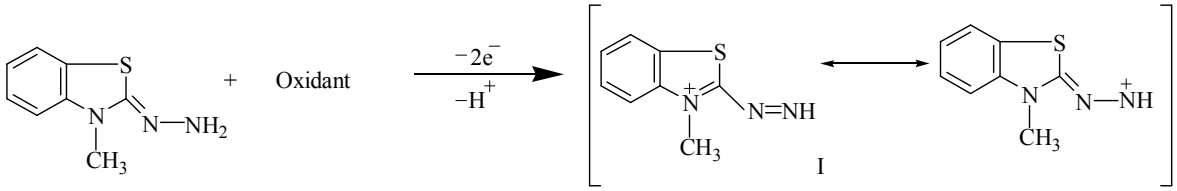
Method B:

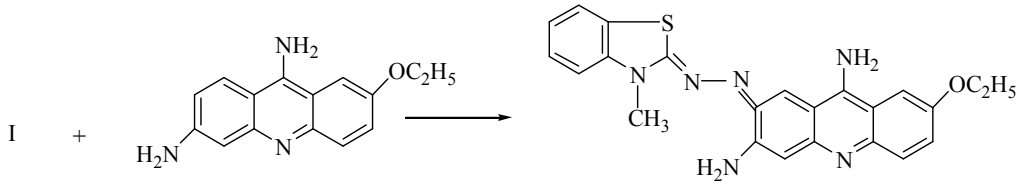
Aliquots of Ethacridine lactate solution (100 µg/ml) ranging from 0.2 to 0.8 ml were transferred into a series of 10 ml volumetric flasks and total volume in all flasks was adjusted to 1.0 ml with water. To each flask 1 ml of 5N hydrochloric acid and 1 ml of odium nitrite solution were added and allowed to stand for five minutes. One ml of ammonium sulphamate solution was then added, mixed and allowed to stand for two minutes. To this solution 1 ml of N-(1-napthyl) ethylenediamine dihydrochloride (B.M reagent) solution was added and mixed well. The final volume was made up to 10 ml with distilled water. The absorbance of pink coloured chromogen was measured at 540 nm against reagent blank. The amount of Ethacridine lactate was computed from calibration curve.

Results and Discussion:

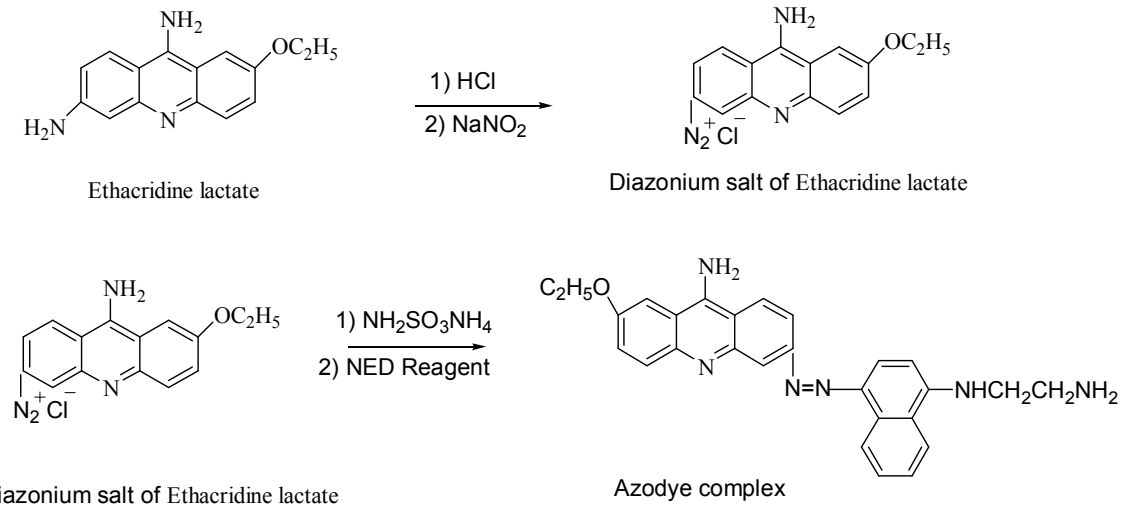
Method A based on oxidative coupling of Ethacridine lactate with MBTH in the presence Of Fe(III). Under the reaction conditions, MBTH on oxidation with Fe(III), loses two electrons and one proton forming an electrophilic intermediate nwhich has been postulated to be the active coupling species. One mole of this intermediate reacts wih ethacridine lactate by an electrophilic attack on the most electrophilic site of ethacridine lactate to form a coloured species. The mechanism of formation of colored products had beenshown in scheme no 1

.Ethacridine lactate contains two primary aromatic amine functional groups. We developed method B based on diazotization of primary aromatic amine of Ethacridine lactate with nitrous acid (generated insitu) followed by coupling with B.M. reagent The mechanism of formation of colored products had been shown in scheme no 2.





Scheme.No-1



Scheme.NO - 2

Table-1: Optical characteristics and regression analysis parameters

Parameter Method-A Method-B

PARAMETER	M_A	M_B
λ_{max} (nm)	535	540
Beer's law limits (μg ml^{-1})	2– 8	2 – 8
Detection limits (μg ml^{-1})	0.272	0.050
Molar absorptivity (l $mole^{-1}$ cm^{-1})	3.29×10^4	2.37×10^4
Sandell's sensitivity (μg cm^{-2} / 0.001 absorbance unit)	0.011	0.014
Optimum photometric range (μg ml^{-1})	3-7	4 – 10.5
Regression equation (Y = a + bC)*		
Slope (b)	0.095×10^{-2}	6.82×10^{-2}
Standard deviation of slope (S_b)	1.29×10^{-3}	0.14×10^{-3}
Intercept (a)	1.4×10^{-2}	-0.40×10^{-3}
Standard deviation of intercept (S_a)	7.84×10^{-3}	1.15×10^{-3}
Standard error of estimation (S_e)	1.08×10^{-2}	1.10×10^{-3}
Correlation coefficient (r)	0.9997	0.9999
Relative standard deviation (%)*	0.461	0.165
% Range of error (Confidence limits)**		
0.05 level	0.251	0.138
0.01 level	0.372	0.205
% Error in bulk samples***	0.340	0.128

*y=a+bx, where 'x'is the concentration of ethacridine lactate in μg/ml and y is the absorbance value

** average of six determinations

*** average of three determinations

Table-2: Estimation of Ethacridine lactate in pharmaceutical formulations:

sample	Labeled amount (mg/ml)	Amount found by proposed methods* (mg)±SD		Amount found by reference method (mg)±SD	% Recovery by roposed methods** ±SD	
		Method A	Method B		Method A	Method B
1	1	0.97±0.15	0.98±0.12	0.98±0.011	99.42±0.014	99.56±0.011
2	1	1.02±0.13	1.03±0.14	1.02±0.012	100.02±0.013	100.01±0.012

* Average of six determinations.
** Average of three determinations

The two developed methods follow Beer's law in the concentration range of 2-8 µg/ml. Interference studies were conducted to see the influence of excipients with the proposed methods. The common excipients usually present in dosage forms do not interfere in the proposed method A and method B. The optical characteristics, regression analysis data and precision of the methods are presented in table no 1. The accuracy of the methods was evaluated by estimating the amount of Ethacridine lactate in previously analyzed samples to which known amounts of Ethacridine lactate was spiked. The accuracy of the methods was also conformed by comparison of the results obtained by proposed and reference methods. The results of accuracy were given in table-2. Some of the commercially available formulations were procured from the local market and analyzed by the developed methods and the results comply with the labeled claim (table-2).

Conclusion:

The proposed methods are economic, simple, sensitive, reproducible and accurate and can be used for the routine analysis of Ethacridine lactate in bulk as well as in its pharmaceutical preparations.

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