Research Article

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NEW SPECTROPHOTOMETRIC METHODS FOR THE QUANTITATIVE ESTIMATION OF AZTREONAMIN FORMULATIONS

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Abstract:

Three new spectrophotometric methods were proposed for the Quantative Estimation of Aztreonam. Method A(Tpooo) and Method B(ARS) are based on the fornation of ion association complex with the drug solution and in Method C (PNA Method) diazotization fallowed by coupling with drug in alkaline medium. Linearity ranges and RSD will be 10-70ppm and 0.23 for Method A and 40-120 ppm and 1.044 for Method B and 200-100ppm and 0.28 respectively. All these method are Accurate, precise and very effective even at low concentrations and used for the quantitive estimation of Aztreonam in commercial formulations.

Key Words:

Aztreonam, Tpooo Method, ARS Method, PNA Method, Zithromax.

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Introduction:

Aztreonam is a synthetic monocyclic beta-lactam antibiotic (a *monobactam*), with the nucleus based on a simpler monobactam isolated from *Chromobacterium violaceum*. It was approved by the U.S. Food and Drug Administration (FDA) in 1986. It is resistant to some beta-lactamases, but is inactivated by extended-spectrum beta-lactamases.

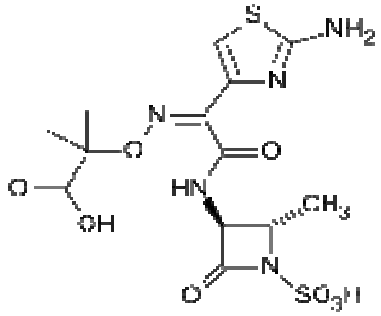

Figure 1: Stricture of Aztreonam

Aztreonam eliminates bacteria that cause many kinds of infection, including pneumonia and gynecological, urinary tract, skin, bone, joint, stomach, and blood infections. This medication is sometimes prescribed for other uses; ask your doctor or pharmacist for more information.

Aztreonam is usually given by injection into a vein or a muscle. The dosage is based on medical condition and response to therapy. Aztreonam is similar in action to penicillin. It inhibits mucopeptide synthesis in the bacterial cell wall, thereby blocking peptidoglycan cross linking. It has a very high affinity for penicillin-binding protein 3 (PBP-3) and mild affinity for PBP-1a. Aztreonam binds the penicillin-binding proteins of gram-positive and anaerobic bacteria very poorly and is largely ineffective against them. Aztreonam is bactericidal but less so than some of the cephalosporins.

Reported side-effects include injection site reactions, rash, and rarely toxic epidermal necrolysis. Gastrointestinal side effects generally include diarrhea and nausea and vomiting. There may be drug-induced eosinophilia. Because of the un-fused beta-lactam ring unique to Aztreonam, there is limited cross-reactivity between Aztreonam and other beta-lactam antibiotics, and it is generally considered safe to administer Aztreonam to patients with hypersensitivity (allergies) to penicillin. Aztreonam is considered Pregnancy category B.

Experimental Procedure:

Reagents and Materials

All chemicals used were of analytical reagent grade and distilled water was used to prepare all solutions. Double beam VVVisible Spectrophotometer is used for measuring the absorbances of the color formed during the analysis.

Preparation of reagents

Tropaeolin-ooo solution: weigh 200 mg of Tropaeolin-ooo (Tpooo) and is dissolved in 100ml of distill water.

HCL Solution: dissolve 8.6 ml of concentrated hydrochloric acid in 1000ml of distill water.

Alizarin red solution: weigh 200mg of Alizarin red (ARS) and is dissolved in 100ml of distill water.

PNA solution: accurately 100 mg of PNA was weighed and was taken in a 100 ml graduated volumetric flask. It was dissolved in 0.2 M HCl solution and made up to the mark.

NaNO2 solution: accurately 100 mg of NaNO2 was weighed and was taken in a 100 ml graduated volumetric flask. It was dissolved in distilled water and made up to the mark.

NaOH solution (4 %, 1M): accurately 4g of NaOH was weighed and was taken in a 100ml graduated volumetric flask. It is dissolved in distilled water and made up to the mark.

Preparation of working standard drug solution

Weigh accurately 10mg of Aztreonam taken in a 10ml calibrated volumetric flask , dissolve with little amount of distill water shaken well and made the solution up to mark. The resultant solution attain 1000ppm concentration (Stock solution 1). Take 1ml from the stock solution 1 and further diluted to 10 ml with distill water. Resulting solution attains 100ppm concentration and is considered as a stock solution 2. Further analysis is carried out by taking the drug from stock solution 2.

Methods

Method A: Tpooo Method

In a series of 125 ml separating funnels containing aliquots of standard drug solution was taken. To this 6ml of HCl solution and 2ml of Tpooo solutions were added successively. The total volume of the aqous phase in each separating funnel was adjusted to 15ml with distill water. To each separating funnel 10ml of Chloroform was added and the contents were shaken for 2 min. the two phases were allowed to separate and the absorbance of the separated chloroform layer was measured at 480nm against a similar reagent blank.

Method B: ARS Method

In a series of 125 ml separating funnels containing aliquots of standard drug solution was taken. To this 6ml of HCl solution and 2ml of ARS solutions were added successively. The total volume of the aqueous phase in each separating funnel was adjusted to 15ml with distill water. To each separating funnel 10ml of Chloroform was added and the contents were shaken for 2 min. the two phases were allowed to separate and the absorbance of the separated chloroform layer was measured at 495nm against a similar reagent blank.

Method C: PNA method

In a 10 ml graduated test tubes 1.0 ml of PNA solution and 1.0 ml of NaNO2 solution were successively added and allowed to stand for 2 min. Later, standard drug of elected concentration is delivered into the test tube. Then 1.5 ml of NaOH solution was added and the volume in each tube was

made up to 10 ml distill water. Solution attains green color. The maximum absorbances were measured 440nm against a reagent blank.

Assay Procedure for Formulations

An amount of finely ground tablet powder equivalent to 100 mg of Aztreonam (Zithromax- 250mg) was accurately weighed into a 100 ml calibrated flask, 60 ml of water added and shaken for 20 min. Then, the volume was made up to the mark with water, mixed well, and filtered using a Whatman No 42 filter paper. First 10 ml portion of the filtrate was discarded and a suitable aliquot of the subsequent portion (1000 µg mL-1 Aztreonam) was diluted appropriately to get suitable concentrations for analysis by proposed methods.

Method Validation:

Selection of analytical concentration ranges: (linearity test)

Linearity test was evaluated by measuring the absorbance values of standard solutions. The standard stock solution of Aztreonam, appropriate aliquots were pipetted out in to a seven series of 10 ml volumetric flasks and make up to 10ml mark with the solutions required for each individual method. After color formation absorbance of each concentration was measured at wavelength found for the proposed method. Results were shown in Table: 1 and Standard graphs of linearity for proposed methods were shown below.

Accuracy and Precision

To evaluate the accuracy and precision of the methods, pure drug solution (Within the working limits) was analyzed and being repeated six times. The relative error (%) and relative standard deviation (%) were less than 2.0 and indicate the high accuracy and precision for the proposed methods (Table 2).

Recovery Studies

To ensure the accuracy and reproducibility of the results obtained, known amounts of pure drug was added to the previously analyzed formulated samples and these samples were reanalyzed by the proposed method and also performed recovery experiments. The Percentage recoveries thus obtained were given in Table 3.

Application to Analysis of Commercial

Sample

In order to check the validity of the proposed methods, Aztreonam was determined in commercial formulation. From the results of the determination it is clear that there is close agreement between the results obtained by the proposed methods and the label claim. These results indicating that there was no significant difference between the proposed methods and the reference methods in respect to accuracy and precision.

Discussion:

In method A and method B, drug being a base form an ion association complex with acid dye Tpooo and ARS respectively. The formed complex is extractable in to Chloroform from the aqueous phase. The protonated nitrogen

positive charge of the drug molecule in acid medium is expected to attack the positive charge of the dye. Hence form a colored complex which is extracted with Chloroform.In method C diazotization of PNA with sodium nitrate fallowed by coupling with drug in alkaline medium. The formed PNA- DRUG complex develop green color, the developed color can be estimated by using spectrophotometer at a wavelength 440 nm.

Conclusions:

Three useful micro methods for the determination of Aztreonam have been developed and validated. The methods are simple and rapid taking not more than 20- 25 min for the assay. These spectrophotometric methods are more sensitive than the existing UV and HPLC methods, and are free from such experimental variables as heating or extraction step. The methods rely on the use of simple and cheap chemicals and techniques but provide sensitivity comparable to that achieved by sophisticated and expensive technique like HPLC. Thus, they can be used as alternatives for rapid and routine determination of bulk sample and tablets.

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Tables

Parameter	Tpooo method	ARS method	PNA method
Wavelength Max	480nm	495nm	440nm
Correlation coefficient	0.999	0.999	0.998
Slope	0.018	- 0.013	0.012
Intercept	- 0.008	0.007	0.016
RSD of Precision	0.023	1.04	0.28
Average Recovery	99.35	99.87	100.38
%of Assay for formulation	99.68	99.89	98.2

Table 1: summery of the proposed methods for Aztreonam

S.No	Tpooo method (Abs at 40ppm)	ARS method (Abs at 80ppm)	PNA method (Abs at 60ppm)
1	0.712	1.07	0.774
2	0.711	1.08	0.775
3	0.712	1.05	0.777
4	0.714	1.06	0.774
5	0.715	1.07	0.778
6	0.711	1.05	0.779
RSD	0.23	1.044	0.28

Table 2: Precision test results.

Method	Recovery	Conc. In ppm	Amount of Aztreonam recovered(ppm)	% Recovery	Mean recovery
Tpooo method	50%	10	9.85	98.5	99.35
	100%	20	9.95	99.5	
	150%	30	30.017	100.05	
ARS method	50%	40	39.94	99.85	99.87
	100%	80	79.91	99.88	
	150%	120	119.86	99.88	
PNA method	50%	20	20.07	100.35	100.38
	100%	40	40.16	100.4	
	150%	60	59.88	99.8	

Table 3: Result of Recovery studies

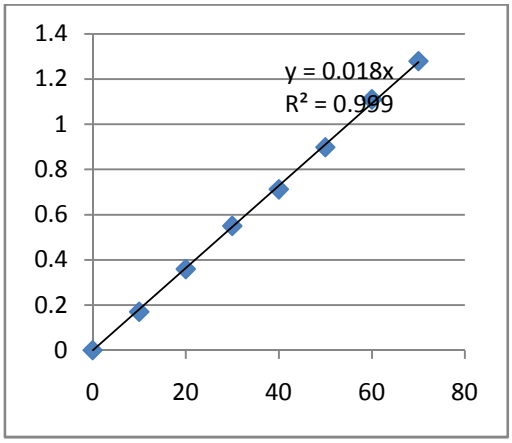
Formulations

S.NO	Method	Formulation	Amount Prepared	Amount Found	% Asssay
1	Tpooo	Zithromax Tablet 250mg	40ppm	39.87	99.68
2	ARS Method		80ppm	79.91	99.89
3	PNA Method		60 ppm	58.92	98.2

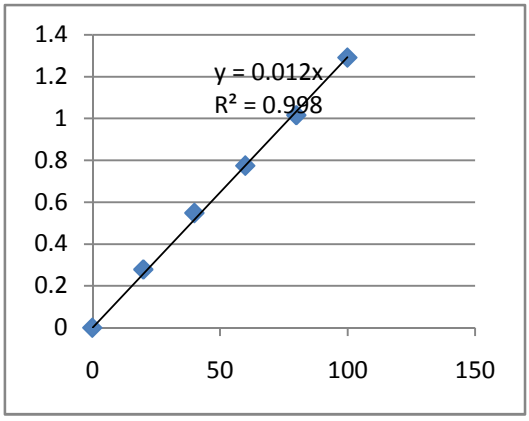
Table 4: formulation study results.

Graphs

Tpooo Method



PNA Method



ARS Method