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Optimized UV-Vis spectrophotometric method for estimation of anastrozole in pharmaceutical solid dosage form

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ABSTRACT

A simple and valuable UV Spectrophotometric method was developed for anastrozole in bulk and in its pharmaceutical formulation using different solvent. The maximum absorbance (λmax) was found to be 263nm for acetate buffer (P^H2.8). The calibration curve was in concentration range 10-50µg/ml. due its simplicity, rapidness, high precision and accuracy this method may be applied successfully for determining anastrozole in bulk and on tablet dosage formulation. The repeatability study was done for the precision of proposed method. All the results of analysis were validated according to the International Conference on Harmonization (ICH) guideline. This method has been successfully used to determine Anastrozole content in tablets of different origin and bulk mixtures.

Key words: Anastrozole, Spectrophotometric assay

INTRODUCTION

Anastrozole chemically is known as 2-[3(1-cyano-1-methyl-ethyl)-5-(1H-1, 2, 4-triazole-1-yl-methyl) phenyl]-2-methyl-propinenitrile is a potent and selective aromatase inhibitor. It is a white crystalline solid, odourless and is freely in methanol, acetone, ethanol, tetrahydrofuran, and very soluble in acetonitrile having melting point 81-82 degree Celsius [3, 4].

Anastrozole is indicated for adjuvant treatment and for first –line treatment of postmenopausal women with hormone receptor-positive early breast cancer or hormone receptor unknown locally advanced or metastatic breast cancer [5].anastrozole is indicated for treatment of advanced breast cancer in postmenopausal women with disease progression following tamoxifen therapy and even in patients with ER negative disease.[6] Anastrozole is not official in IP, USP and BP. The review of literature reveals that only few chromatographic methods have been reported for the estimation of anastrozole like LCMS, LCNMR MS, capillary gas chromatography, HPLC. [7-10]. There is a need for developing newer methods in UV for developing a simple and economic method and so we proceeded with UV and validated as per the ICH guidelines. This thesis deals with the investigation carried out in laboratory on the development and validation of UVspectroscopical method for determination of anastrozole.

In the present investigation an attempt has been made to develop accurate and precise UV spectrophotometric method for the estimation of Anastrozole in bulk and pharmaceutical formulations. The method is potentially suitable for drug monitoring and determination of pharmacokinetic profiles .

MATERIALS AND METHODS

Materials

Spectrophotometer analysis was carried out on a Shimadzu(pharmaspec-1700) U.V. visible spectrophotometer and systronic-2210 U.V. visible double beam spectrophotometer with spectral bandwidth of 2 nm and a pair of 1cm

quartz cells. Pure drug samples of Anastrozole were procured as a gift sample from Dabur India Limited,Sahibabad,U.P. Tablets (Altraz, Alkhem Pvt. Ltd.) containing Anastrozole (1mg) were procured from local market.

Selection of solvent

Different solvents are tried for obtaining UV spectra for anastrozole. The peak absorbance were compared among the solventsas shown in table- 1.Among the five solvents, acetate buffer ph 2.8 shows greater absorbance 0.385 at λmax 263nm. Due to greter absorbance shown by acetate buffer ph 2.8 was chosen as the solvent system for estimation of anastrozole.

TABLE-1 Selection of solvent for anastrozole

Concentration (µg/ml)	solvent	solubility	λmax (nm)	Absorbance
10	Acetate buffer ph3.4	Not soluble	Not identified	Noise
10	Buffer solution ph2.5	Sparingly soluble	Not identified	Noisy
10	Phosphate buffer ph 2.0	Not soluble	Not identified	Noisy
10	Phosphate buffer ph2.5	Not soluble	Not identified	Noisy
10	Acetate buffer ph 2.8	Soluble	263	.385

Preparation of Standard Stock Solution

Standard solution of stock solution was prepared by dissolving 5mg of drug in 10ml of solvent (acetate buffer ph 2.8) to get concentration of 500µg/ml solutions.

Scanning and determination of maximum wavelength(λmax)

In order to ascertain the wavelength of maximum absorption(λmax)of the drugs(100µg/ml and 6µg/ml)in acetae buffer ph 2.8 are scanned using spectrophotometer within the wavelength region of 200-400 nm against acetate buffer ph 2.8 as blank. The resulting spectra were shown in fig -1 and the absorption curve showed characteristic absorption maxima at 263nm for anastrozole.

Construction of calibration curve

For construction of beer's law plot for anastrozole aliquots were taken separately in 10ml volumetric flask and the volume was made up to the mark with solvent (acetate buffer ph 2.8) to prepare a series of solution contain10-50 µg/ml.the absorbance of all the above solutions were measured at 263nm and the calibration curve was plotted by taking concentration of drug on X-axis the absorbance on Y-axis and was shownm in figure-2. The drug has obeyed beer's law in the concentration range 20-50µg/ml. Results of analysis of tablets were shown in Table-2.

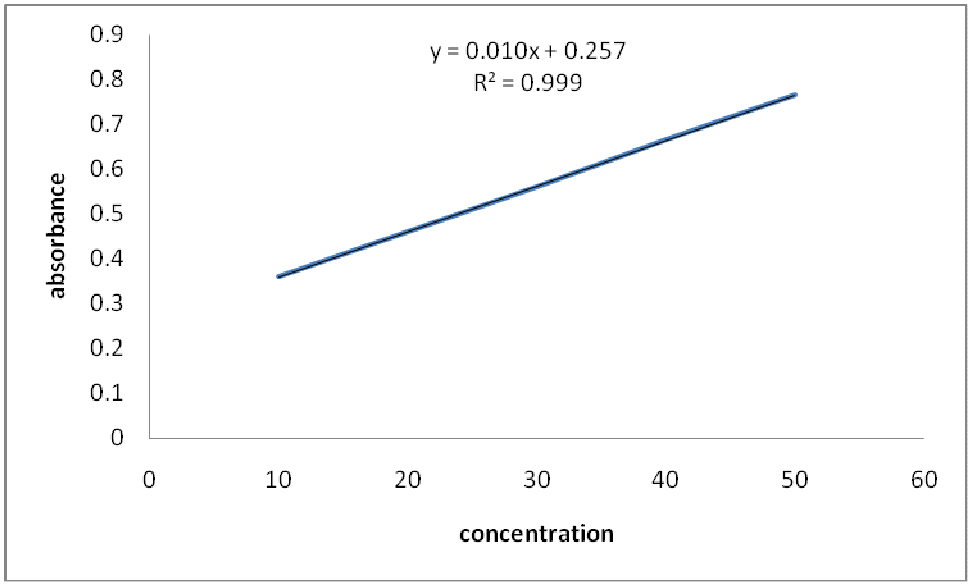

Table-2: linearity table of anastrozole

Sl.no.	Concentration(µg/ml)	Absorbance
1	10	0.360
2	20	0.460
3	30	0.560
4	40	0.665
5	50	0.765

Preparation and Analysis of Tablet Sample

For analysis of commercial formulation content, 20 tablet of brand of anastrozole were accurately weighted and average weight of powder per tablet were determined separately and mixed thoroughly. Drug equivalent to 1mg of anastrozole was accurately weighted and dissolved in 25 ml solvent (acetate buffer ph2.8). then the solution was sonicated for 30 minutes and filtered. From that solution 7.5 ml was taken and diluted to 10 ml with that of solvent to get 30µg/ml.further three dilution (10-30µg/ml) were made and their absorbance were measured at 263nm and concentration was determined from regression equation of calibration curve.Results of analysis of tablets were shown in Table-3. .

Table-3: Results of analysis of tablets

Formulation	Labeled amount of Anastrozole(µg/ml)	Amount obtained(µg)	% of drug present	% RSD
Altraz (Alkem)	1000	999.95±0.051	99.99	0.0053

**Each value is average of three determinations ± Standard deviation*

Validation of Method

The method was validated in terms of linearity, accuracy, precision, specificity and reproducibility of the sample applications. The linearity of the method was investigated by serially diluting the stock solution of Anastrozole and measuring the absorbance values at 263 nm. Calibration curves were constructed by plotting absorbances against concentrations of drug in µg/ml.

Precision:

The precision of the proposed method was ascertained by actual determination of eight replicates of fixed concentration of the drug within the Beer's range and finding out the absorbances by the proposed method.From these absorbances Mean,Standard deviation ,% RSD and percentage range of errors (at 0.05 and 0.01 confidence limits) was calculated. The readings were shown in Table-4.

TABLE-4: Intraday and inter day precision of determination of anastrozole

Amount taken(µg/ml)	10	20	30	40	50
Intraday variation amount found (µg/ml)	10.13	20.05	30.03	40.18	50
%found	101.30± 0.0012	100.25± 0.0018	100.12± 0.0015	100.46± 0.0010	100.00± 0.0014
%bias	1.300	0.250	0.100	0.450	0
%RSD	0.335	0.393	0.269	0.152	0.185
Interday variation amount found(µg/ml)	9.93	20.03	29.98	40.13	50
%found	99.37± 0.0014	100.15± 0.0014	99.95± 0.0014	100.34± 0.0021	100.00± 0.0012
%bias	-0.700	0.150	-0.067	0.325	0
%RSD	0.393	0.306	0.251	0.319	0.158

**each value is average of three determination ±standard deviation.*

TABLE-5: Recovery study of pure drug using tablet formulation

SAMPLE ID	CONCENTRATION OF ANASTROZOLE		ABSORBANCE OF PURE DRUG AND FORMULATION	% RECOVERY OF PURE DRUG	STATISTICAL ANALYSIS
	PURE DRUG (µg/ml)	PARENTERAL FORMULATION(µg/ml)			
S_1:80%	24	30	0.502	99.81	MEAN:99.86 S.D:0.0942 %RSD:0.0944
S_2:80%	24	30	0.504	100.00	
S_3:80%	24	30	0.503	99.80	
S_4:100%	30	30	0.560	100.00	MEAN:100.05 S.D:0.0801 %RSD:0.0800
S_5:100%	30	30	0.560	100.00	
S_6:100%	30	30	0.561	100.17	
S_7:120%	36	30	0.671	99.85	MEAN:99.85 S.D.:0.1224 %RSD:0.1226
S_8:120%	36	30	0.670	99.70	

ACCURACY

For validity and reproducibility of the proposed method, recovery studies were carried out. A known amount of the standard drug was added to pre-analyzed tablet solution sample, at three levels (80 %, 100 %, 120 %) and the resulting solutions were analyzed by the proposed method. Percentage recoveries were calculated and results are presented in Table 5.

RESULTS AND DISCUSSION

Anastrozole chemically is known as 2-[3(1-cyano-1-methyl-ethyl)-5-(1H-1, 2, 4-triazole-1-yl-methyl) phenyl]-2-methyl-propinenitrile is a potent and selective aromatase inhibitor. It is a white crystalline solid, odourless and is freely in methanol, acetone, ethanol, tetrahydrofuran, and very soluble in acetonitrile having melting point 81-82 degree Celsius Anastrozole is indicated for adjuvant treatment and for first –line treatment of postmenopausal women with hormone receptor-positive early breast cancer or hormone receptor unknown locally advanced or metastatic breast cancer .anastrozole is indicated for treatment of advanced breast cancer in postmenopausal women with disease progression following tamoxifen therapy and even in patients with ER negative disease. Anastrozole is not official in IP, USP and BP. The review of literature reveals that only few chromatographic methods have been reported for the estimation of anastrozole like LCMS, LCNMR MS, capillary gas chromatography, HPLC. There is a need for developing newer methods in UV for developing a simple and economic method and so we proceeded with UV and validated as per the ICH guidelines. This work deals with the investigation carried out in laboratory on the development and validation of UVspectroscopical method for determination of anastrozole.

From the optical characteristics of the proposed method it was found that the drug obeys linearity within the concentration range 10-50µg/ml.The slope and intercept was found to be 0.010 and 0.257 for acetate buffer ph 2.8.From the precession table for acetate buffer ph 2.8 the %RSD value was found to be less than 1% which indicate that the proposed method has found reproducibility.It was found that the percentage recovery values of pure drug from the analyzed formulation was 99.81-100.17 for acetate buffer ph 2.8 The system suitability parameter also reveals that the values were within the specified limits for acetate buffer ph 2.8

These proposed methods were found to be simple, precise, accurate and sensitive.high percentage recover showed that the method was free from interference of excipients used in the formulation. Values LOD and LOQ showed that the proposed method was sensitive enough to analyse the drug in bulk as well as in it's pharmaceutical formulation. Hence the proposed method renders suitable for routine analysis in quality control laboratory.
The results are presented in Table 6.

Table-6: Optical characteristic and stratified data

Parameters	Anastrozole
Absorption maximum(nm)	263
Beeer's law(µg/ml)	10-50
Molar absorptivity	0.0219×10^{4}
Send cell's sensitivity (µg/cm^2/0.001)	50.067×10^{-3}
%relative standard deviation	0.2668
%range of error 0.05 confidence limit 0.01 confidence limit	 0.158 0.121
Limit of detection(LOD)	0.414
Limit of quantitation(LOQ)	1.38
Correlation coefficient(R^2)	0.999
Slope(m)	0.010
Intercept(c)	0.257

CONCLUSION

The proposed method was found to be simple,precise,accurate and sensitive.High percentage recovery showed that the method was free from interference of excipients used in the formulation.Values of LOD and LOQ showed that the proposed method was sensitive enough to analyze the drug in bulk as well as in its pharmaceutical formulation.Hence the proposed method renders suitable for routine analysis in quality control laboratories.

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