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RESEARCH ARTICLE

Analytical Techniques for the Determination of Erlotinib HCl in Pharmaceutical Dosage Forms by Spectrophotometry

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Abstract: Three simple, rapid and sensitive spectrophotometric methods were developed for the determination of Erlotinib hydrochloride in pharmaceutical formulations. Beer's law was obeyed over a concentration range 0.5-30 µg/mL in HCl and acetate buffer and 1-30 µg/mL in phosphate buffer. The linear regression equations were found to be $y = 0.0717x + 0.0083$, $y = 0.0676x + 0.0102$ and $y = 0.0638x + 0.0096$ in HCl, acetate buffer and phosphate buffer respectively and the three methods were validated as per ICH guidelines.

Keywords: Erlotinib HCl, Spectrophotometry, Validation

Introduction

Erlotinib HCl is chemically *N*-(3-ethynylphenyl)-6, 7-bis (2-methoxyethoxy) quinazolin-4-amine (Figure 1) with molecular weight of 429.90 g/mol[1]. Erlotinib specifically targets the epidermal growth factor receptor tyrosine kinase, which is highly expressed and occasionally mutated in various forms of cancer. It binds in a reversible fashion to the adenosine triphosphate (ATP) binding site of the receptor[2]. It is approved for the treatment of patients with locally advanced or metastatic non-small cell lung cancer which belongs to 4-anilinoquinazoline class of compounds[3]. Its monotherapy has demonstrated clinical activity in non-small cell cancer, head and neck cancer and ovarian cancer in Phase studies in USA[4-6].

Erlotinib HCl was determined by different analytical techniques such as liquid chromatography-mass spectrometry[7-11] and liquid chromatography[12-16] methods in biological samples, Spectrophotometry[17-19], spectrofluorimetry[20-21], UPLC[22], HPTLC[23] and RP-HPLC[24-30] in pharmaceutical formulations.

In the present study, three novel simple, rapid and cost-effective UV spectrophotometric methods were developed for the routine analysis of Erlotinib HCl in pharmaceutical formulations in 0.1 N hydrochloric acid (Method A), acetate buffer pH 4.0 (Method B) and phosphate buffer pH 5.0 (Method C) and they are validated as per the ICH guideline[31].

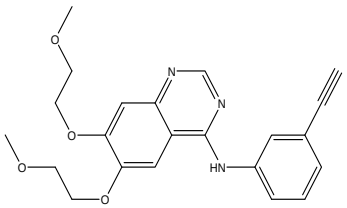

Figure 1. Chemical structure of Erlotinib HCl

Experimental

A double beam UV-VIS spectrophotometer (UV-1800, Shimadzu, Japan) connected to computer loaded with spectra manager software UV Probe was employed with spectral bandwidth of 1 nm and wavelength accuracy of ±0.3 nm with a pair of 10 mm matched quartz cells. For scanning, the wavelength range selected was 400 nm to 200 nm with medium scanning speed. All weights were taken using electronic balance (Denver, Germany). All experiments were performed at room temperature (25±1) °C.

Reagents and chemicals

Analytical grade reagents were used. Pure samples of Erlotinib HCl was kindly supplied as gift sample from Dr. Reddy's Labs (India) India. Erlotinib HCl is available commercially as tablets with brand names TARCEVA ®, ERLOCIP and TYROKININ ® (containing 100 mg and 150 mg of the drug content) respectively and twenty tablets from each brand were procured from the local market.

Preparation of hydrochloric acid (0.1 N) (Method A)

8.5 ml of conc. Hydrochloric acid was taken in a 1000 mL volumetric flask and diluted up to the mark with distilled water.

Preparation of acetate buffer (pH 4.0) (Method B)

2.86 mL of glacial acetic acid and 1.0 mL of a 50 per cent solution of sodium hydroxide were taken in a 1000 mL volumetric flask, add diluted up to the mark with distilled water.

Preparation of phosphate buffer (pH 5.0) (Method C)

6.8 grams of potassium di hydrogen phosphate was taken in 1000 mL of water and adjusted pH to 5.0 with 10 M potassium hydroxide.

Preparation of stock solution

Erlotinib HCl stock was prepared by dissolving 25 mg of the drug in methanol in 25 mL volumetric flask (1000 µg/mL) and dilutions were made from the stock solution with hydrochloric acid, acetate buffer and phosphate buffer for method A, B and C respectively. The above solutions were scanned (200- 400 nm) against their reagent blank and the absorption spectra were recorded for method A, B and C respectively.

Linearity

A series of drug solutions were prepared for method A, B (0.5-30.0 µg/mL) and C (1-30 µg/mL) and scanned (200- 400 nm) against their reagent blank. The absorbance of the above solutions was noted from the absorption spectra recorded for the three methods A, B and C respectively and a calibration curve was plotted by taking the concentration of the solutions on the x-axis and the corresponding absorbance on the y-axis.

Precision and accuracy

The precision study was done by recording the absorbance of six replicates for method A, B and C (20 µg/mL) and the %RSD was calculated. Accuracy was evaluated from the percent recovery studies by the addition of 80%, 100% and 120% of pure sample solution to the pre-analysed formulation solution. Erlotinib HCl extracted drug solution from the formulation (10 µg/mL) was spiked with 80%, 100% and 120% of pure API solution and the % recovery was calculated.

Assay procedure for the commercial formulations

Twenty tablets from each brand were procured from pharmacy store and extracted using methanol. The filtrate so obtained during the extraction was diluted further with hydrochloric acid, acetate buffer and phosphate buffer separately for method A, B and C respectively and the percentage recovery was calculated.

Results and Discussion

The absorption spectrum of Erlotinib in hydrochloric acid (Method A) has shown two λ_{max} values at 248.18 and 342.37 nm (Figure 2) but λ_{max} 342.37 nm was chosen for all the analytical determinations.

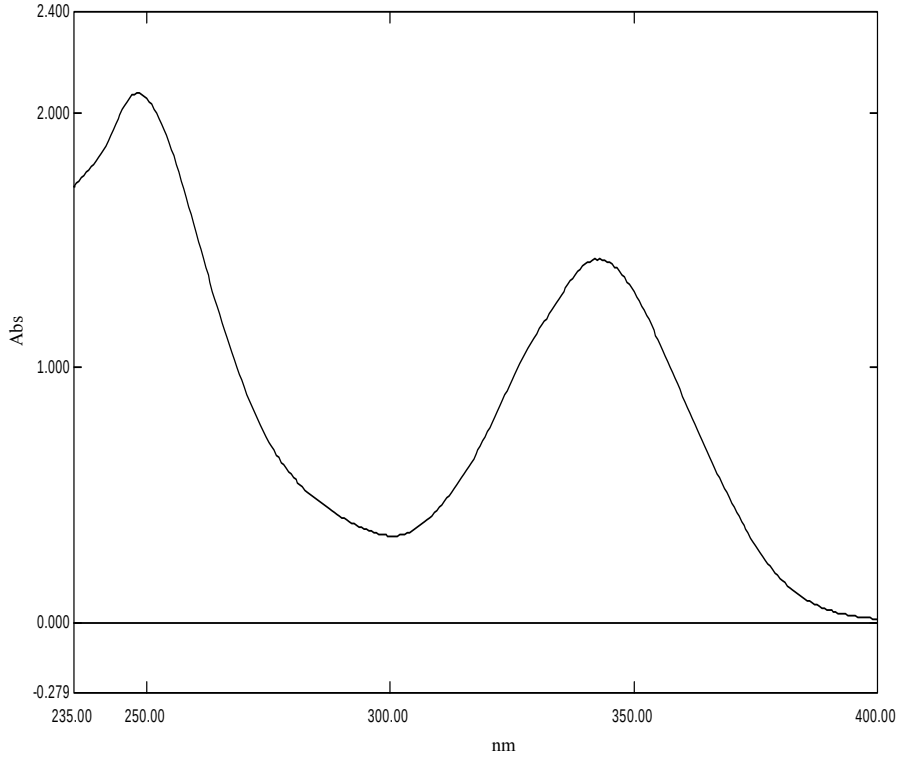

Figure 2. Absorption spectrum of Erlotinib in HCl (20 µg/mL)

Similarly the absorption spectrum of Erlotinib has shown λ_{max} at 342.40 nm in acetate buffer (Figure 3) (Method B) and at λ_{max} 340.94 nm in phosphate buffer (Figure 4) (Method C).

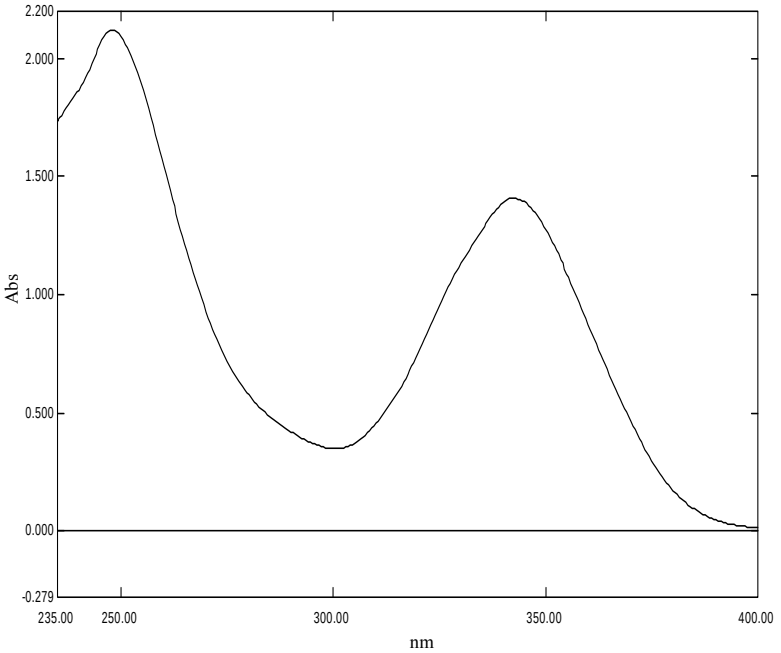

Figure 3. Absorption spectrum of Erlotinib in acetate buffer (20 µg/mL)

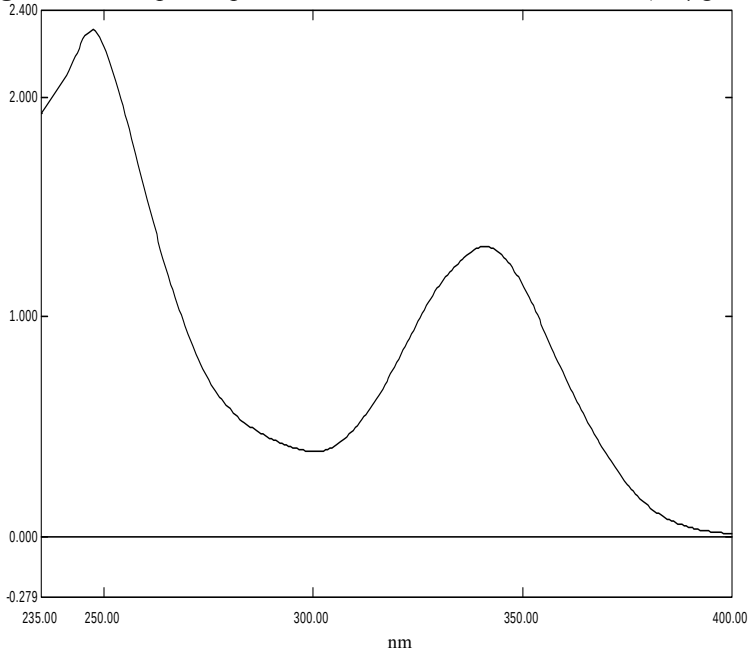

Figure 4. Absorption spectrum of Erlotinib in phosphate buffer (20 µg/mL)

A graph was drawn by taking the concentration of the drug solutions on the x-axis and the corresponding absorbance values on the y-axis for the data obtained in method A, B and C and the calibration curves were shown in Figure 5. The linear regression equations were

found to be y = 0.0717x + 0.0083 (R^2= 0.9992), y = 0.0676x + 0.0102(R^2= 0.999) and y = 0.0638x + 0.0096(R^2= 0.999) in method A, B and C respectively. The % RSD in precision studies was found to be less than 2% in method A (0.23-0.56), B (0.54-0.63) and C (0.38-0.68) indicating that the methods are more precise. The optical characteristics were shown in Table 1.

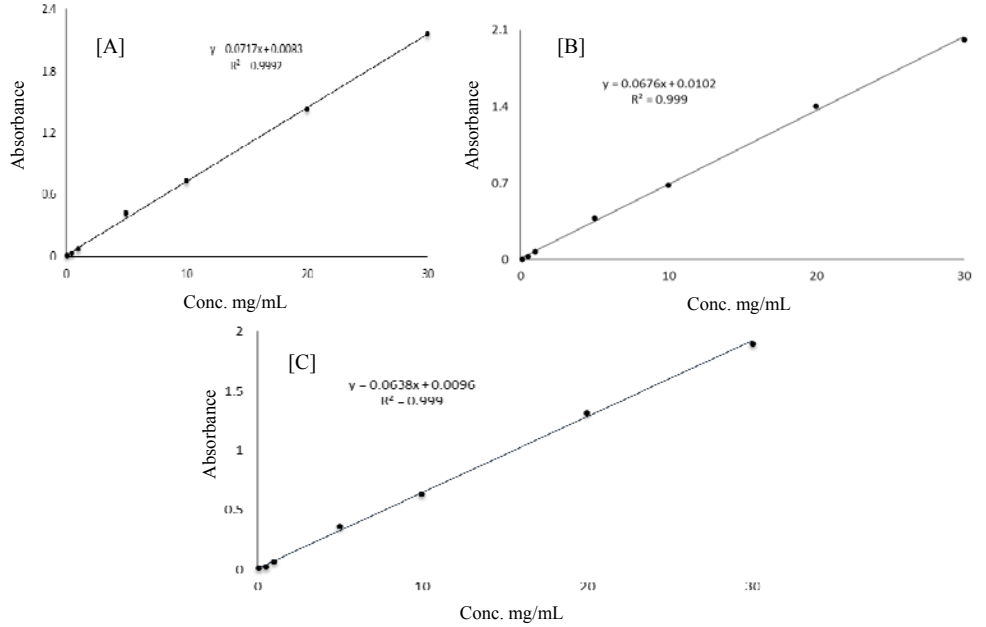

Figure 5. Calibration curves of Erlotinib in A) Hydrochloric acid B) Acetate buffer and C) Phosphate buffer

Table 1. Optical characteristics of Erlotinib HCl

Parameters	Method A	Method B	Method C
λ_{max}, nm	342.37	342.40	341.08
Linearity range, µg/mL	0.5-30	0.5-30	1-30
Molar extinction coefficient (L/mol/cm)	$3.13827x10^3$	$2.92332x10^3$	$2.738463x10^3$
Sandell's sensitivity (µg/cm^2 /0.001 Abs unit /0.001 Abs unit)	0.013699	0.014706	0.015699
Slope	0.0717	0.0676	0.0638
Intercept	0.0083	0.0102	0.0096
Correlation coefficient	0.9992	0.999	0.999
Precision (%RSD)			
Intra-day (n=3)	0.23	0.63	0.38
Inter-day (n=3)	0.56	0.54	0.68
Accuracy (% recovery)	99.74-99.85	99.46-99.91	99.32-99.7

The % RSD in accuracy studies was also found to be less than 2.0 indicating that the methods are accurate. The percentage recovery was found to be 99.68-99.88, 99.89-99.94 and 99.84-99.89 for methods A, B and C respectively in marketed formulations (Table 2).

Table 2. Analysis of Erlotinib HCl commercial formulation (Tablets)

Brand	Labeled amount mg	Amount obtained mg			% Recovery			% RSD		
		Method			Method			Method		
		A	B	C	A	B	C	A	B	C
I	100	99.68	99.89	99.84	99.68	99.89	99.84	0.32	0.42	0.68
II	100	99.88	99.92	99.86	99.88	99.92	99.86	0.55	0.39	0.31
III	100	99.83	99.94	99.89	99.83	99.94	99.89	0.49	0.28	0.55

Conclusion

The proposed methods are simple, precise and accurate and can be applied for the determination of Erlotinib hydrochloride in pharmaceutical formulations successfully.

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