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New spectrophotometric techniques for the estimation of osimertinib mesylate in tablet dosage form

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ABSTRACT

Osimertinib Mesylate is used for a treatment of non small cell lung cancer (NSCLC). Whereas only few simple, precise and accurate spectrophotometric methods were developed for the determination of Osimertinib Mesylate (tagrisso) in pharmaceutical dosage forms. The absorption maxima was found to be at 267 nm in method A (0.1N HCl) and shows linearity over the concentration range of 0.002-0.02 µg/mL with regression equation y=0.4323x + 0.0104 (r^2 = 0.9992). In Method B (Sodium acetate buffer, pH 4.5) the drug obeys Beer Lambert's law (λ_{max}267nm) in the concentration range of 0.002-0.02 µg/mL with regression equation y=0.484x-0.017(r^2= 0.9992). In Method C (phosphate buffer, pH 7.2) the drug obeys Beer Lambert's law (λ_{max}267nm) in the concentration range of 0.002-0.02 µg/mL with regression equation y=0.2949x+0.0108(r^2= 0.9992) In Method D (Methanol) the drug obeys Beer Lambert's law (λ_{max}267nm) in the concentration range of 0.002-0.02 µg/mL with regression equation y=0.6323x+0.003 (r^2= 0.999). 1st derivative spectrophotometric method (E, F, G and H) were developed in 0.1NHCl and Sodium acetate pH 4.5 and phosphate buffer pH 7.2 and methanol in which Osimertinib Mesylate obeys Beer Lambert's law 0.002-0.02 µg/mL and 0.002-0.02 µg/mL and 0.002-0.02 µg/mL and 0.002-0.02 µg/mL with regression equations y=0.0259x + 0.0008 and y=0.0137x - 0.0005 and y=0.0097x-0.0008 and y=0.0087-0.0007 respectively. The proposed spectrophotometric method was validated as per the ICH guidelines and can be applied for the determination of Osimertinib Mesylate in pharmaceutical formulations. Osimertinib Mesylate, Derivative spectroscopy, Spectrophometry, Validation, Tagrisso.

Keywords: Tagrisso, Osimertinib Mesylate, Derivative spectroscopy, Spectrophometry, Validation.

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1. INTRODUCTION

Osimertinib Mesylate (recently known as mereletinib; exchange name Tagrisso) is a drug used to treat non little cell lung carcinomas with an explicit change. It is a third-age epidermal development factor receptor tyrosine kinase inhibitor. Created by astrazeneca, the prescription was affirmed as a malignancy treatment in 2017 by both the nourishment and medication organization and the European commission.

Osimertinib Mesylate is a little atom tyrosine kinase receptor inhibitor and antineoplastic operator that is utilized in the treatment of chose types of cutting edge non-little cell lung malignant growth (NSCLC). Osimertinib Mesylate is related with a moderate rate of serum aminotransferase rises amid treatment and uncommon cases of clinically obvious intense liver damage.

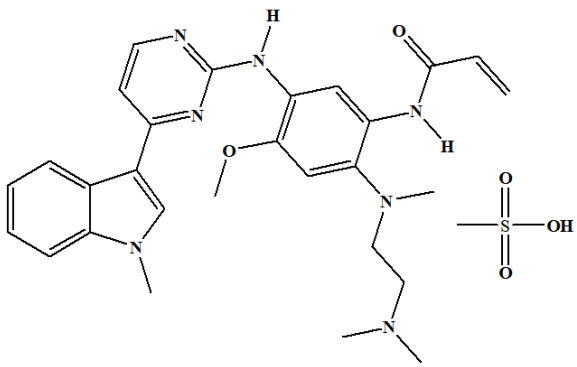


Figure 1: Structure of Osimertinib Mesylate

2. MATERIALS AND METHODS

2.1 Instrumentation

A double beam UV-VIS spectrophotometer (UV-1800, Shimadzu, Japan) connected to a computer loaded with spectra manager software UV Probe was employed with a spectral bandwidth of 1nm and wavelength accuracy of **±** 0.3 nm with a pair of 10 mm path length matched quartz cells. All weights were taken on the electronic balance (Shimadzu). For scanning, the wavelength range selected was 400nm to 200nm with medium scanning speed.

2.2 Chemicals and reagents

HPLC grade Methanol (Merck), glacial acetic acid (Merck), sodium acetate trihydrate (Merck), Hydrochloric acid (Rankem) potassium Di-hydrogen phosphate (Merck), and sodium hydroxide (Merck) was used. Osimertinib Mesylate, obtained as a gift sample from

2.3 Preparation of 0.1N HCl

Add 4.25mL of 35% Conc. Hydrochloric acid (Hcl) was added to the 500mL volumetric flask containing 450mL of distilled water or de-ionised water and mixed well. The volume was then made up to 500mL of water.

2.4 Preparation of Sodium Acetate Buffer (pH 4.5)

Weigh accurately Sodium acetate trihydrate (1.48 gm) in a 500ml volumetric flask containing 500ml distilled water and mixed well, then 1.7mL glacial acetic acid (GAA) was added to it and the pH adjusted to 4.5 with respectively to glacial acetic acid.

2.5 Preparation of phosphate buffer pH 7.2

6.8grams of potassium Di-hydrogen phosphate and 1.4grams of sodium hydroxide were weighed accurately and was added in a 1000ml volumetric flask containing 900ml deionized water and mixed well. The volume was made up with water to 1000ml.

2.6 Preparation of stock solution

The standard solution of Osimertinib Mesylate was prepared by dissolving accurately about 10 mg of the Osimertinib Mesylate with methanol in a 10 ml volumetric flask.

The stock solution was further diluted with 0.1N HCl and pH 4.5 sodium acetate buffer for method A (0.002-0.02µg/mL) and method B (0.002-0.02µg/mL) and pH 7.2 phosphate buffer for method C (0.002-0.02µg/mL) and methanol buffer for method D (0.002-0.02µg/mL) respectively as per the requirement.

2.7 Procedure for preparation of the calibration curve

The drug solutions were scanned (200-400 nm) against the reagent blank (0.1N HCl for method A and sodium acetate buffer pH 4.5 for method B and phosphate buffer pH 6.8 for method C and phosphate buffer pH 7.2 for method D) and the absorption spectra were recorded. The absorption maximum (λ_{max}) was observed at 267 nm for method A, B, C and D. The absorption spectra so obtained were converted in to first derivative spectra by the inbuilt software of the instrument and the resulting spectrum shows both maxima and minima and therefore the magnitude of the amplitude was recorded against concentration for method E, F, G and H. Calibration curves were constructed by taking the concentration of the drug solutions on the x-axis and the corresponding absorbance values on the y-axis.

2.8 The assay procedure for the marketed formulations (Tablets)

Osimertinib Mesylate Mesyalate is available with brand name Tagrisso (0.5 mg and 1mg of the drug per tablet; America Pharmaceuticals Inc.) were purchased from the local market. Twenty tablets average weight was calculated and crushed into fine powder. Osimertinib Mesylate equivalent to 25 mg was weighed, extracted with methanol by sonication for 40 minutes with intermittent shaking and makeup to volume with methanol in 250 ml volumetric flask (0.1mg/mL) and centrifuged at 4000rpm for 10 minutes to collect the supernatant for further dilutions. The dilutions were made from this stock as per the requirement for method A, B, C and Dand the percentage recovery was calculated.

2.9 Precision and Accuracy

The precision and accuracy studies as per the ICH guidelines were performed. The absorbance of six replicates (0.01 µg /mL) for Method A and E, (0.045µg/mL) for Method B and F, (0.050µg/mL) for Method C and G, (0.065µg/mL) for Method D and H were noted and the % RSD was calculated.

Accuracy was evaluated as per the ICH guidelines by the percent recovery studies by the addition of 50%, 100%, and 150% of Osimertinib Mesylate solution extracted from the formulation was taken and the % RSD was calculated.

3. RESULTS

New spectrophotometric methods were developed for the determination of Osimertinib Mesylate in pharmaceutical preparations. Osimertinib Mesylate has shown absorption maxima (λ_{max}) at 214 nm in 0.1N HCl (Method A) and Sodium acetate buffer pH 4.5 (Method B) and phosphate buffer pH 7.2 (Method C) and methanol (Method D) the corresponding absorption spectra were shown in Figures,

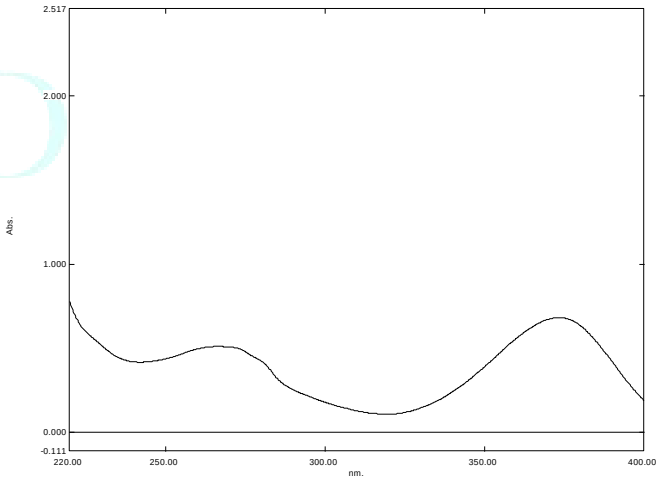


Figure 2: Absorption spectrum of Osimertinib Mesylate (1.0 µg /mL) in 0.1N HCl

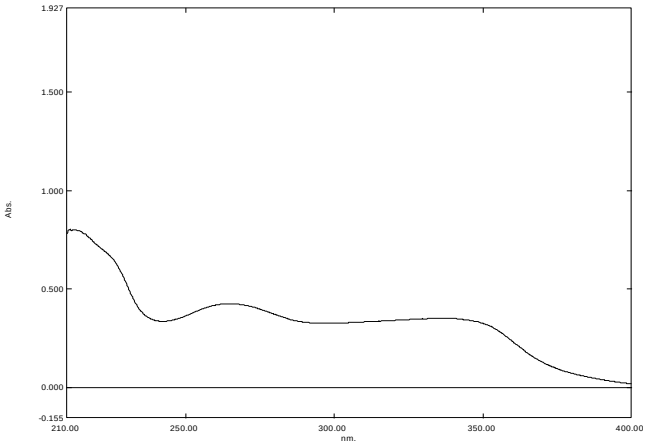


Figure 3: Absorption spectrum of Osimertinib Mesylate (1.0 µg /mL) in pH 4.5 Acetate Buffer

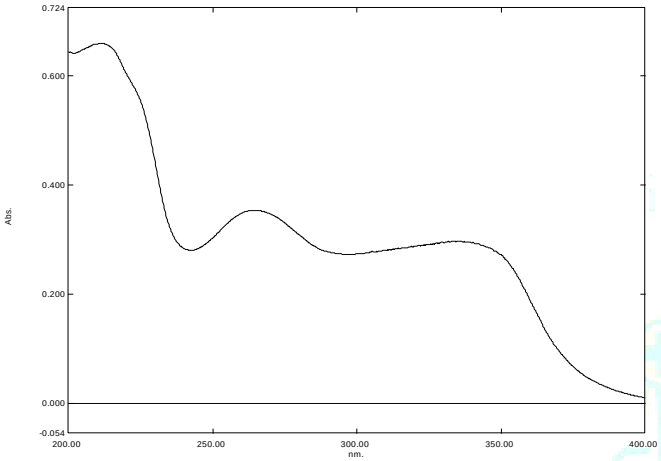


Figure 4: Absorption spectrum of Osimertinib Mesylate (1.0 µg /mL) in pH 7.2 Phosphate Buffer

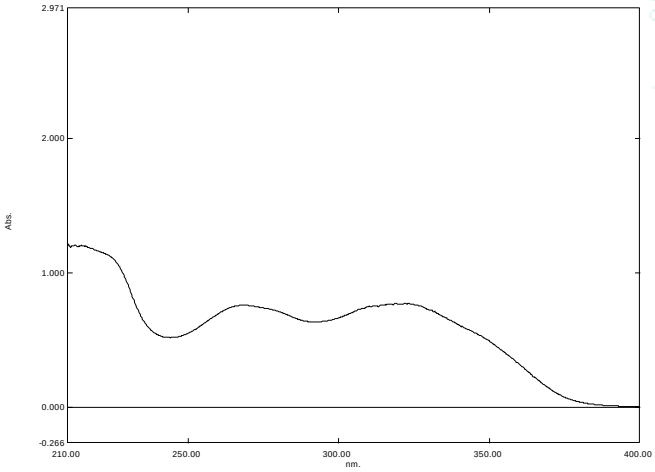


Figure 5: Absorption spectrum of Osimertinib Mesylate (1.0 µg /mL) in Methanol

In method E, Osimertinib Mesylate has shown zero crossing points at 241.55, 267.36, and 373.41 nm, with maxima at 255.21 nm and minima at 283.19 nm in Figure 6 and therefore the amplitude has been taken against the concentration for the construction of the calibration curve. Similarly, in method F, Osimertinib Mesylate has shown zero crossing point at 242.47, 265.09, 298.07 and 334.69 with maxima at 252.18 nm and minima at 276.86 nm in Figure 7 and therefore the amplitude has been taken against the concentration for the construction of the calibration curve. Similarly, in method G, Osimertinib Mesylate has shown zero crossing point at 201.95, 212.06, 242.50, 265.07, 297.52, 334.28, 334.71 and 335.00 with maxima at 252.19 nm and minima at 276.80 nm in Figure 8 and therefore the amplitude has been taken against the concentration for the construction of the calibration curve. Similarly, in method H, Osimertinib Mesylate has shown zero crossing point at 202.74, 246.05, 266.69, 295.51 and 316.98with maxima at 257.60 nm and minima at 282.92 nm in Figure 9 and therefore the amplitude has been taken against the concentration for the construction of the calibration curve

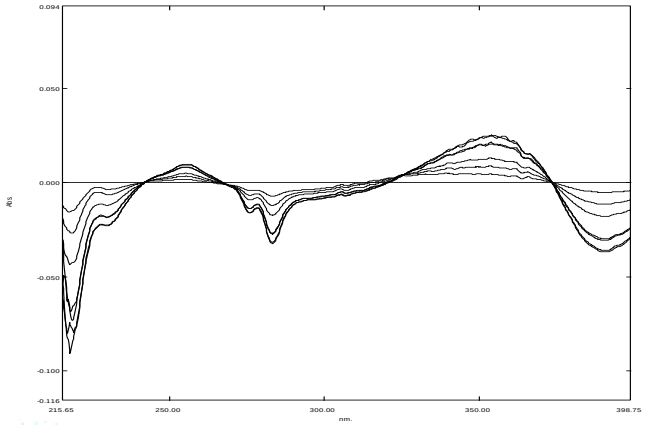


Figure 6: Overlay first derivative spectra (D_1) of Osimertinib Mesylate in 0.1N HCl

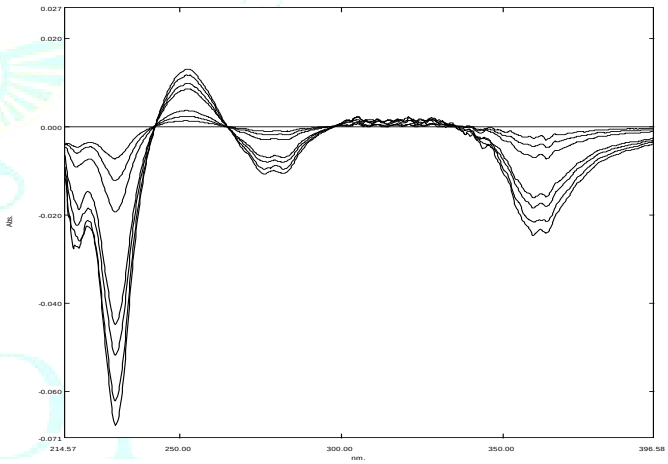


Figure 7: Overlay first derivative spectra (D_1) of Osimertinib Mesylate in pH 4.5 Acetate buffer

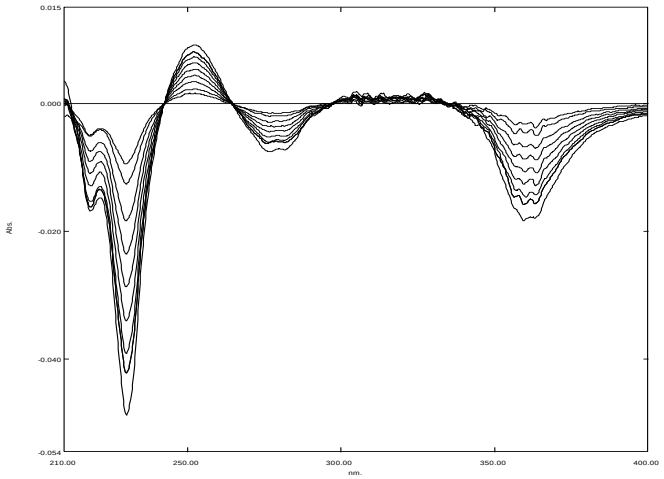


Figure 8: Overlay first derivative spectra (D_1) of Osimertinib Mesylate **in pH 7.2 phosphate Buffer**

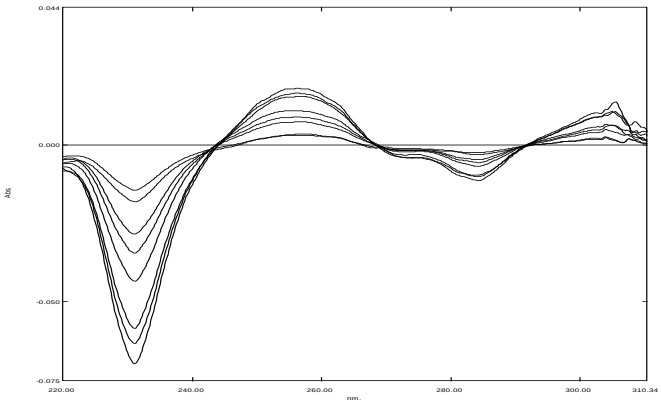
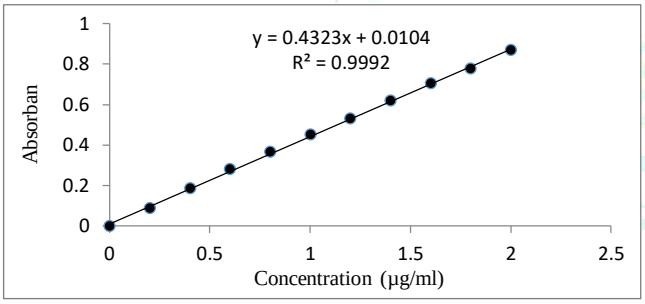
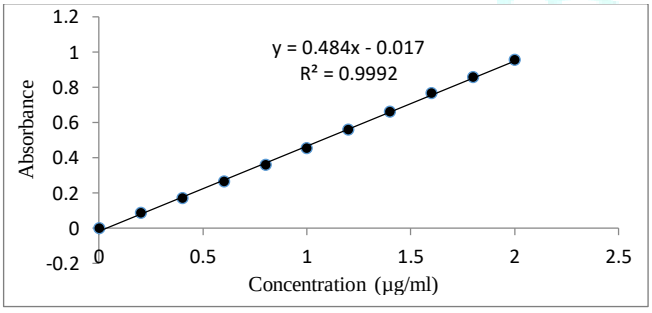


Figure 9: Overlay first derivative spectra (D_1) of Osimertinib Mesylate in methanol

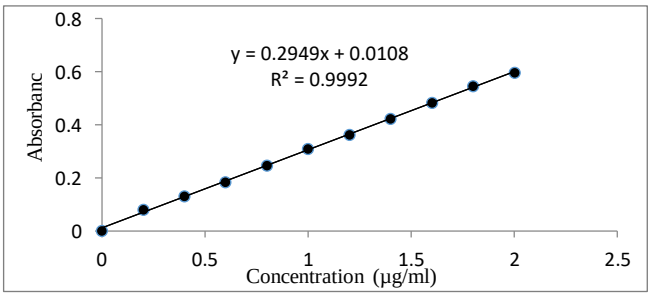
Beer's law was obeyed in the concentration range of 0.002-0.02 µg / mL for method A and E and 0.002-0.02 µg/mL for Method B and F and 0.002-0.02 µg/mL for Method C and G and 0.002-0.02 µg/mL for Method D and H. The linear regression equations were found to be y = 0.4323x + 0.0104, y = 0.0259x + 0.0008, y = 0.484x - 0.017, y = 0.0137x - 0.0005, y=0.2949x+0.0108, y=0.0097x-0.0008, y=0.6323x+ 0.003 and y=0.0087x-0.0007 for method A, B, C, D, E, F, G and H respectively (Figure 6) with correlation coefficient 0.9994, 0.9991, 0.9993, 0.9994, 0.9992, 0.9992, 0.9992 and 0.999 respectively (Table 1).



(A)



(B)



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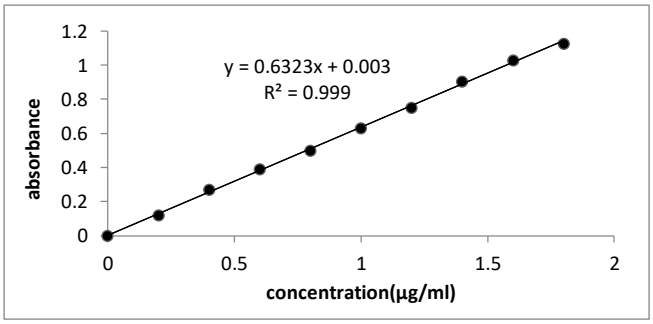
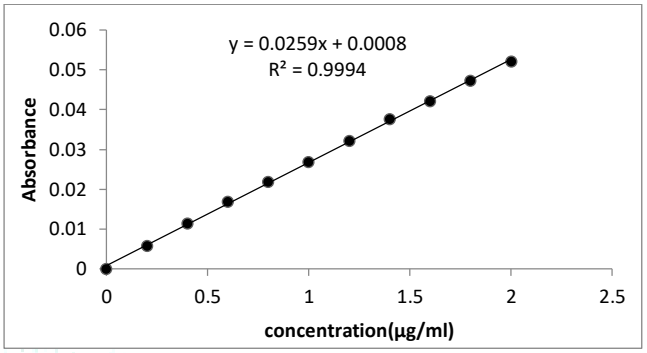
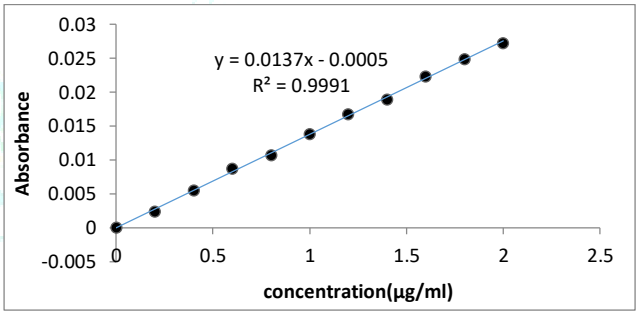


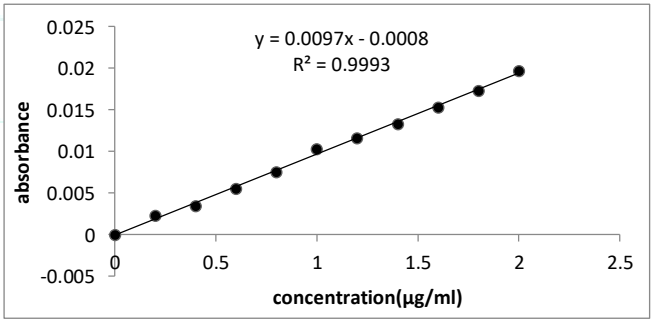
(D)



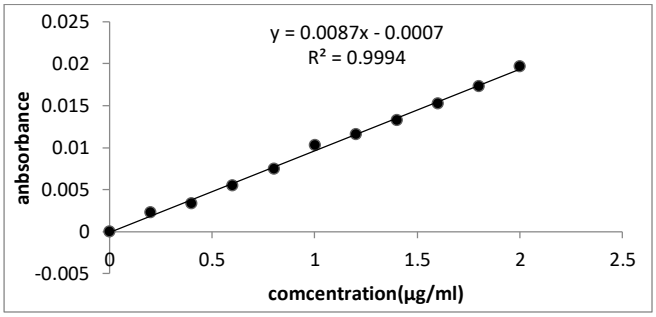
(E)



(F)



(G)



(H)

Figure 10: Calibration curves of Osimertinib Mesylate in method A, B, C, D, E, F, G and H

Table 1: Optical characteristics of Osimertinib Mesylate

Parameters	Method							
	A	B	C	D	E	F	G	H
Beer-Lambert's limits (µg /mL)	0.002-0.02	0.002-0.02	0.002-0.02	0.002-0.02	0.002-0.02	0.002-0.02	0.002-0.02	0.002-0.02
λ_{max}/Amplitude range (nm)	267	267	267	267	255.30-283.30	252.34-276.88	252.01-276.80	257.66-282.91
Regression equation	0.4323x+0.0104	0.484x-0.017	0.2949x+0.0108	0.6323x+0.003	0.0259x+0.0008	0.0137x-0.0005	0.0097x-0.0008	0.0087x-0.0007
Slope	0.4323	0.484	0.2949	0.6323	0.0259	0.0137	0.0097	0.0087
Intercept	0.0104	0.017	0.003	0.003	0.0008	0.0005	0.0008	0.0007
Correlation coefficient	0.9992	0.9992	0.9992	0.999	0.9994	0.9991	0.9993	0.9994
Sandells Sensitivity	2.49* 10^{-5} µgcm^{-2}	1.97* 10^{-5} µgcm^{-2}	3.28* 10^{-5}µgcm^{-2}	1.00* 10^{-5} µgcm^{-2}	4.52* 10^{-4} µgcm^{-2}	7.09* 10^{-4} µgcm^{-2}	1.19* 10^{-4} µgcm^{-2}	3.57* 10^{-4} µgcm^{-2}

The % RSD values in precision studies were found to be 0.12, 0.28, 0.34, 0.24, 0.57, 0.69 and 0.91 for method A, B, C and D respectively (RSD <2%) indicating that the method is more precise. The % Recovery values (Table 2) were found to be 99.10%, 99.23%, 99.34%, 99.44%, 99.32%, 99.12%, 99.47% and 99.50% with RSD 0.13, 0.39, 0.45, 0.56, 0.35, 0.68 and 0.74 for method A, B, C and D respectively (RSD <2%) indicating that the proposed methods can be applied for the determination of pharmaceutical formulations and the method is more accurate.

LOQ is defined as the lowest amount of analyte which can be detected. LOD was defined as the lowest amount of analyte which can be quantitatively determined. LOD and LOQ of the drug were calculated as per ICH guidelines. The Limit of Detection and Limit of Quantification was found to be 0.25µg/ml and 0.825µg/ml (Method A and E) and 0.6µg/mL and 1.98µg/mL (Method B and F) and 0.2µg/ml and 0.66µg/ml (Method C and G) and 0.3µg/ml and 0.99µg/ml (Method D and H) respectively.

Table 2: Assay of API

Level	*Amount obtained (mg)							
	Method							
	A	B	C	D	E	F	G	H
50	0.4939	0.4944	0.4955	0.4964	0.4957	0.4954	0.4966	0.4943
100	0.9949	0.9910	0.9961	0.9972	0.9932	0.9940	0.9953	0.9964
150	0.9965	0.9930	0.9979	0.9986	0.9951	0.9979	0.9961	0.9975

Table 3: Assay of API

Level	% Recovery*							
	Method							
	A	B	C	D	E	F	G	H
50	99.10	99.23	99.34	99.44	99.32	99.12	99.47	99.50
100	99.41	99.12	99.51	99.64	99.31	99.40	99.61	99.71
150	99.61	99.20	99.62	99.71	99.59	99.50	99.79	99.80

DISCUSSION

The objective of the analytical procedure is to govern the validation characteristics which need to be evaluated. Typical validation characteristics which should be considered are listed below: Linearity, Accuracy, Precision, LOD, and LOQ. The linear regression data for the calibration plot were indicative of a good linear relationship between peak area and concentration over a wide range. The results have shown best recoveries (98-102%) of the spiked drug at each added concentration, indicating that the method was accurate. The precision of Osimertinib Mesylate was evaluated and the percentage relative standard deviation (%RSD) was found to be less than 2% which proves that the method was precise. And the Limit of Detection and Limit of Quantification was found to be 0.25µg/ml and 0.825µg/ml (Method A and E) and 0.6µg/mL and 1.98µg/mL (Method B and F) and 0.2µg/ml and 0.66µg/ml (Method C and G) and 0.3µg/ml and 0.99µg/ml (Method D and H) respectively. Hence the proposed method was sensitive.

CONCLUSION

The present methods can be employed for the determination of Osimertinib Mesylate in pharmaceutical formulations successfully and there is no interference of excipients during the study.

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AUTHORS CONTRIBUTIONS

All the authors contributed equally'

CONFLICT OF INTEREST

The authors have no conflict of interest.

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