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VALIDATED RP HPLC METHOD DEVELOPMENT FOR EXEMESTANE IN TABLET DOSAGE FORM

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ABSTRACT

The aim of this present work was to develop stability indicating LC method, which is selective, accurate, simple, precise, reliable, cost effective and rapid for the quantification of all possible degradants and determination of exemestane. In addition, to develop and validate Stability Indicating Method for the determination of impurities (degradation products) in exemestane API by RP-HPLC. Finally, validate the developed method as per ICH guidelines.

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INTRODUCTION:

The principle of chromatographic methods consists in the unequal distribution of components of a mixture between the stationary and the mobile phase. The prerequisite for an unequal distribution is the different possibility of diffusion into them[1-3].

- **Classification of Chromatography:**

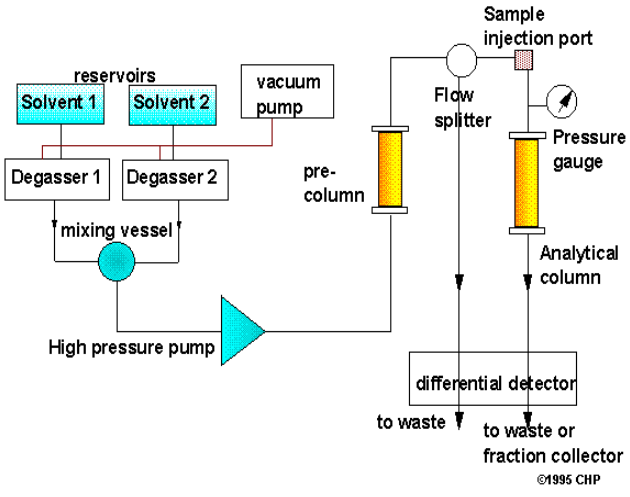

Figure 2: Various components of HPLC are as follows

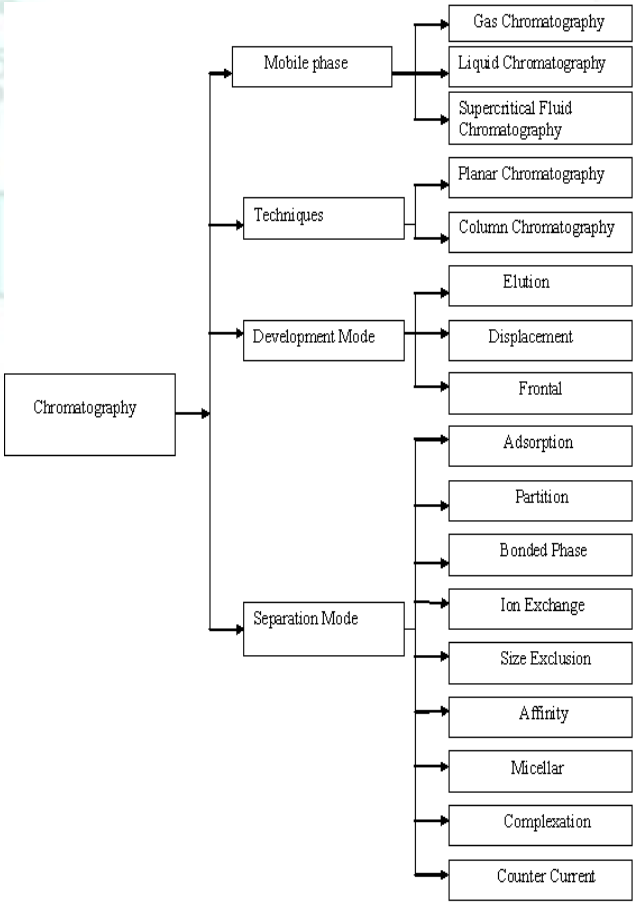

Figure 1: Types of chromatography

Method Development in HPLC

Method development and optimization in liquid chromatography is still an attractive field of research for theoreticians (researchers) and attracts also a lot of interest from practical analysts. "Optimized column, mobile phase, best detection wavelength, efforts in separation can make a world of difference, while developing HPLC method for routine analysis. Determining the ideal combination of these factors assures faster delivery of desired results and a validated method of separation[3-5].

MATERIALS AND METHODS:

Exemestane was received from Cadila Healthcare, Ahmedabad, HPLC grade acetonitrile was purchased from Merck Specialities Private Limited, Mumbai, India. Double distilled water along with acetonitrile was used as diluent throughout the study.

-Selection of Analytical Technique

- HPLC method

- Selection of method for evaluation (either Reverse Phase Chromatography or Normal Phase Chromatography)

-Method development and validate for determination of impurities (degradation products) and of exemestane by using RP-HPLC.

-Selection of different stress studies:

As per ICH guidelines Q1A (R2), different stress conditions were selected and applied to drug for forced degradation studies.

-Validation of method which involves. Specificity

Accuracy. Linearity. Precision.Robustness. Limit of Detection (LOD), Limit of Quantitation (LOQ), Compilation of data.

RESULT AND DISCUSSION:

Selection of Mobile phase

Different mobile phase systems like methanol: water, acetonitrile: water were tried in order to determine the best composition for separation of exemestane. It was found that acetonitrile: water (60:40 % v/v) by isocratic elution gives good resolution and satisfactory peak symmetry as compared to others. Finally this mobile phase was found to be most suitable. The chromatogram obtained by using acetonitrile: water (60:40 %v/v) as mobile phase is shown below in Fig. 3.

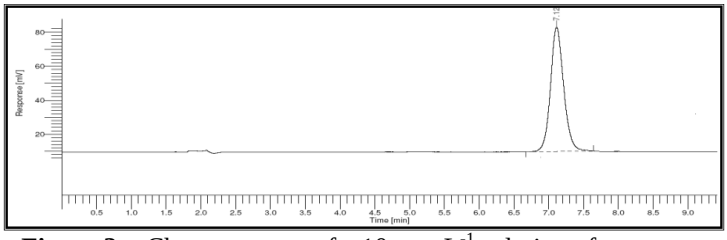

Figure 3: Chromatogram of a 10 µgmL^{-1} solution of exemestane

Calibration Curve

Table shows the peak area observed for various concentrations of standard exemestane solutions. The graph of Peak Area (µV*sec) vs. Concentration (ppm) was plotted in figure.

Table 1: Standard calibration curve for exemestane

S. N.	Concentration (ppm)	Peak Area (µV*sec)
1.	4	584173.86
2.	6	792628.08
3.	8	966578.04
4.	10	1171116.28
5.	12	1353103.47
6.	14	584173.86

Method development

Detection wavelength for the HPLC study was selected as 242 nm. The chromatographic conditions were optimized for resolution of the peak of the drug and degradation products under each forced degradation condition by varying the proportion of acetonitrile/water in the mobile phase. Subsequently, a mixture of samples of different stress conditions was used to optimize the chromatographic conditions for resolving exemestane and all the degradation products in a single run. An appropriate blank was injected before the analysis of all forced degradation samples. Such an optimized method was then used to study the forced degradation behavior of exemestane and was also applied in the determination of exemestane.

Method Validation

Linearity: Peak areas obtained with respective concentrations were subjected to the least square linear regression analysis to calculate the calibration equations and correlation coefficients. The calibration plot for exemestane assay was linear over the calibration range 6–14 µgmL^{-1} and the regression coefficient, slope and intercept were found to be 0.9997,96854 and 4147.6 respectively (In Table). The calibration curve of exemestane is shown below in Fig.

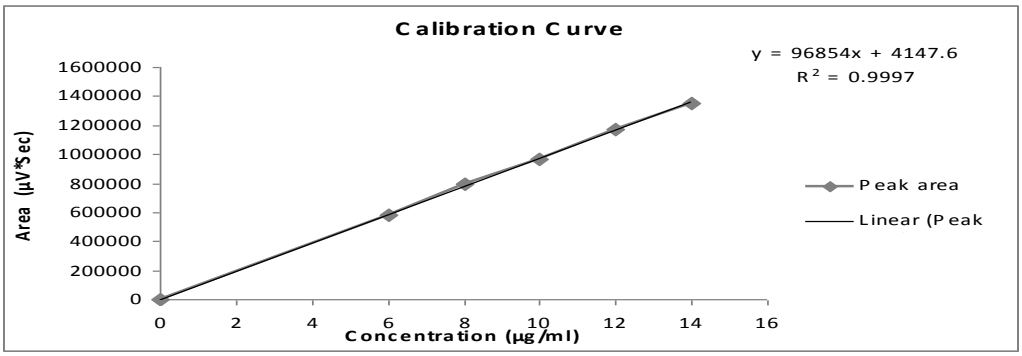

Figure 4: Calibration curve of exemestane

Table 2: Linearity range, slope, intercept and correlation coefficient for Calibration curve

Drug	Linearity range (μgmL^{-1})	Slope	Intercept	Correlation coefficient
Exemestane	4-14	96854	4147.6	0.9997

CONCLUSION:

The analytical method described in this paper is suitable for determination of exemestane and this method has been demonstrated to be accurate, linear, precise, repeatable, specific, and robust, and therefore suitable for routine analysis of exemestane.

This method is a stability indicating method because it can separate all known degradation products from exemestane (API).

The stability indicating method that has been reported in the literature uses 100% organic modifier as the mobile phase and by this method drug has an retention time of greater than 20 min which is costly and time consuming. So, this present method was found to be cost effective and rapid.

From the results of the forced degradation studies it can be concluded that drug was found to degrade rapidly by oxidation, followed by base hydrolysis, acid hydrolysis, dry heat and neutral catalyzed degradation.

As the method is successfully validated using ICH guidelines, it can be readily implemented in quality control laboratories for the purpose of lot release and stability testing of Exemestane API.

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