INTERNATIONAL JOURNAL OF PHARMACEUTICAL RESEARCH AND NOVEL SCIENCES

IJPRNS

A NEW UPLC METHOD FOR THE ESTIMATION OF EXEMESTANE IN PHARMACEUTICAL DOSAGE FORM

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ABSTRACT

A new precise, accurate, rapid method has been developed for the estimation of Exemestane pharmaceutical dosage form by UPLC. From results the proposed method is highly sensitive, precise and accurate and it successfully applied for the quantification of API content in the commercial formulations of Exemestane. A simple and selective UPLC method is described for the determination of ExemestaneChromatographic separation was achieved on aPhenomenex C18 (250×4.6 ×5µ) using mobile phase consisting Acetonitrile:Water:Triethylaminebuffer (60: 40: 0.5%) v/vwith detection of 264 nm. Linearity was observed in the range 50-150 µg /ml for Exemestane(r^2 =0.999) for the amount of drugs estimated by the proposed methods was in good agreement with the label claim.

KEY WORDS: Exemestane, pharmaceutical dosage form, UPLC

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INTRODUCTION

Chromatography is a non-destructive procedure for resolving a multi-component mixture of traces, minor or constituents in to individual fractions. It is a method of separating a mixture of components in to individual components through a porous medium under the influence of solvent. For many years, researchers have looked at “fast LC” as a way to speed up analyses. The need for speed, the availability of affordable and easy to use mass spectrometers. Smaller columns and faster flow rates (amongst other parameters) have been used. Elevated temperature, having the dual advantages of lowering viscosity, and increasing mass transfer by increasing the diffusivity of the analytes, has also been investigated. However, using conventional particle sizes and pressures, limitations are soon reached and compromises must be made, sacrificing resolution. HPLC technology simply doesn’t have the capability to take full advantages of sub-2µm particles. UPLC can be regarded as new invention for liquid chromatography. UPLC refers to Ultra Performance Liquid Chromatography. UPLC brings dramatic improvements in sensitivity, resolution and speed of analysis can be calculated. It has instrumentation that operates at high pressure than that used in HPLC & in this system uses fine particles(less than 2.5µm) & mobile phases at high linear velocities decreases the length of column, reduces solvent consumption & saves time. According to the van Deemter equation, as the particle size decreases to less than2.5 µm, there is a significant gain in efficiency, while the efficiency

does not diminish at increased flow rates or linearvelocitiesTherefore by using smaller particles, speed and peak capacity (number of peaks resolved per unit time in gradient separations) can be extended to new limits, termed Ultra Performance Liquid Chromatography, or UPLC
The technology takes full advantage of chromatographic principles to run separations Using columns packed with smaller particles(less than2.5µm) and/or higher flow rates for increased speed, this gives superior resolution and sensitivity.
Exemestane is a medication used to treat breast cancer. It is a member of the class of antiestrogens known as aromatase inhibitors. Some breast cancers require estrogen to grow. Those cancers have estrogen receptors (ERs), and are called ER-positive. They may also be called estrogen-responsive, hormonally responsive, or hormone-receptor-positive. Aromatase is an enzyme that synthesizes estrogen. Aromatase inhibitors block the synthesis of estrogen. This lowers the estrogen level and slows the growth of cancers. Exemestane is an oral steroidal aromatase inhibitor that is used in ER-positive breast cancer in addition to surgery and/or radiation in post-menopausal women.The main source of estrogen is the ovaries in premenopausal women, while in post-menopausal women most of the body's estrogen is produced via the conversion of androgens into estrogen by the aromatase enzyme in the peripheral tissues (i.e. adipose tissue like that of the breast) and a number of sites in the brain. Estrogen is produced locally via the actions of the aromatase enzyme in these peripheral tissues where it acts locally. Any circulating estrogen in post-menopausal women as well as men is the result of estrogen escaping local metabolism and entering the circulatory system. Exemestane is an irreversible, steroidal aromatase inactivator of type I, structurally related to the natural substrate 4-androstenedione. It acts as a false substrate for the aromatase enzyme, and is processed to an intermediate that binds irreversibly to the active site of the enzyme causing its inactivation, an effect also known as "suicide inhibition." By being structurally similar to enzyme targets, exemestane permanently binds to the enzymes, preventing them from converting androgen into estrogen (1-4).
Analytical method development provides the support to track the quality of the product from batch to batch. Method development involves considerable trial and error procedures. The most difficult problem usually is where to start, what type of column is worth trying with what kind of mobile phase. Single dosage forms with combination of drugs are widely used today due to their advantages and their simultaneous estimation of individual component is a challenging task.

MATERIALS AND METHODS

Preparation of samples for Assay (5, 6)

Preparation of Standard solution

10 mg of Exemestane was weighed and transferred in to 100 ml volumetric flask and dissolved in mobile phase and then make up to the mark with mobile phase and prepare 10 µg /ml of solution by diluting 1ml to 10ml with mobile phase.

Preparation of Sample solution

Weigh 20capsules by removing the shell then crush with mortar and pestlethen weigh a quantity of powder equivalent to 25mg of Exemestane and transferred in to 100 ml volumetric flask and dissolved in mobile phase and then make up to the mark with mobile phase and prepare 10 µg /ml of solution by diluting 1ml to 10ml with mobile phase.

System Suitability& System precision

To verify that the analytical system is working properly and can give accurate and precise results were evaluated by 10µg/mLof Exemestanewas injected six times and the chromatograms were recorded for the same.

RESULTS AND DISCUSSION

The wavelength of maximum absorption (λ_{max}) of the solution of the drug in mobile phase were scanned using UV-Visible spectrophotometer within the wavelength region of 200–400 nm against mobile phase as blank. The

absorption curve shows characteristic absorption maxima at 264 nm for Exemestane. The amount of Exemestane present in the taken dosage form was found to be 99.35 % (Table-1, 2 and fig-1).

Table-1 Results for Exemestane

Exemestane		
	Standard Area	**Sample Area**
Injection-1	54335283	54609367
Injection-2	53884296	54791671
Injection-3	54091715	54876254
Injection-4	54660522	54122289
Injection-5	54144218	54060009
Average Area	54223207	54491918
Assay(%purity)	99.35	

Table -2 Results of assay

Drug	**Label claim(mg)**	**Amount found(mg)**	**% Assay**
Exemestane	25	24.82	99.35

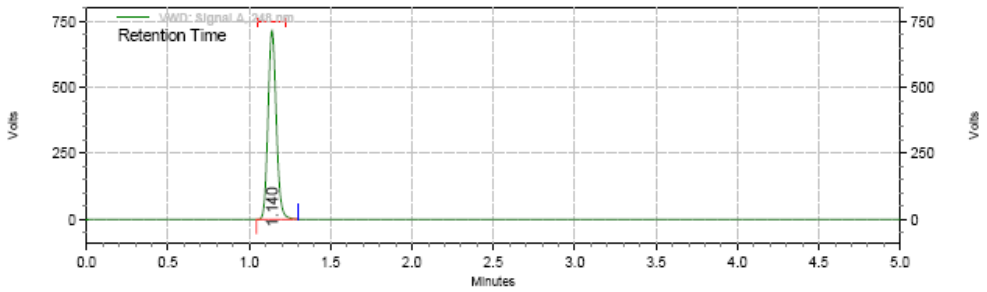

Fig-1 Chromatogram of Assay

The plate count and tailing factor results were found to be within the limits and the % RSD was found to be 0.1 so system is suitable and giving precise results (Table-2).

Table-2 Results for system suitability of Exemestane

Injection	**RT**	**Peak area**	**Theoretical plates (TP)**	**Tailing factor (TF)**
1	1.189	41587410	4578	1.2
2	1.188	41585753	4582	1.1
3	1.190	41585954	4576	1.2
4	1.189	41598374	4852	1.0
5	1.187	41598854	4563	1.1
6	1.191	41588765	4577	1.3
Mean	1.189	415908512	-	-

SD	0.0014	6112	-	-
%RSD	0.11	0.01	-	-

A graph was plotted for Exemestaneagainst the concentrations of the solutions and the peak areas (Table-3). The correlation coefficient R^2 was determined and was found to be 0.999 for Exemestane (Fig-2).

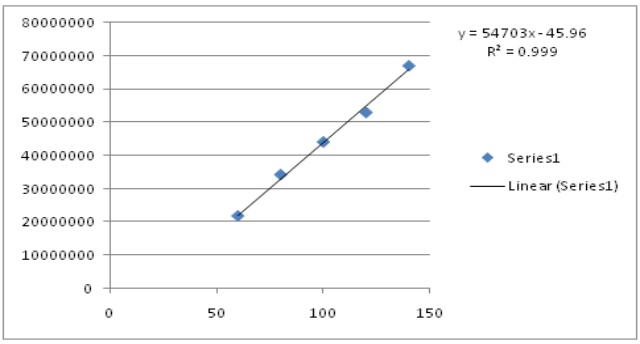

Fig-2 Graph for Linearity data of Exemestane

Table-3 Linearity results of Exemestane

S.No	**Parameter**	**Exemestane**
1	Correlation coefficient	0.999
2	Slope	54703
3	Intercept	45.96

The percentage mean recovery of Exemestane was found between 99.97%. The LOD for this method was found to be 0.368µg/ml (Exemestane). The LOQ for this method was found to be 1.117µg/ml (Exemestane). The results % Assay and %RSD obtained acceptance criteria 2% so method is rugged (Table-4).

Table-4 Ruggedness Results ofExemestane

Exemestane	**%Assay**	Exemestane	**%Assay**
Analyst 01	99.90%	**Analyst 01**	98.56%
Analyst 02	98.25%	**Analyst 02**	99.82%
%RSD	0.45	%RSD	0.78

CONCLUSION

A new precise, accurate, rapid method has been developed for the estimation of Exemestane pharmaceutical dosage form by UPLC. From the above experimental results and parameters it was concluded that, this newly developed method for the estimation Exemestanewas found to be simple, precise, accurate and high resolution and shorter retention time makes this method more acceptable and cost effective and it can be effectively applied for routine analysis in research institutions, quality control department in meant in industries, approved testing laboratories studies in near future. From results the proposed method is highly sensitive, precise and accurate and it successfully applied for the quantification of API content in the commercial formulations ofExemestaneEducational institutions and Quality control laboratories.

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