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DEVELOPMENT AND VALIDATION OF A NEW RP-HPLC METHOD FOR ESTIMATING ERIBULIN MESYLATE IN PHARMACEUTICAL DOSE FORM

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ABSTRACT

In the research analysis a rapid, accurate and reliable High Performance Liquid Chromatography (HPLC) method was developed and validated by selecting chromatographic parameters for the estimation of Eribulin Mesylate in tablet dosage form. The HPLC method was developed using reverse phase Thermosil C_{18} (4.6×100mm) 5µ column with mobile phases containing Phosphate buffer: MeoH (35:65% v/v). The flow rate was 1.0 ml / min with PDA detection at λ max 254 nm with 10min run time. This method has been validated by the use of different validation parameters such as accuracy, precision, linearity and robustness. Such findings showed that the system could find practical use in its tablet dosage forms as a quality assurance tool for evaluating the drug in pharmaceutical industries.

INTRODUCTION

Eribulin, sold under the brand name Halaven, is an anticancer medication used to treat breast cancer and liposarcoma. The most common side effects include fatigue, nausea, hair loss, constipation, certain nerve damage causing weakness or numbness in the hands and feet, abdominal pain and fever. Eribulin may also cause low levels of infection-fighting white blood cells (neutropenia) or decreased levels of potassium or calcium.

METHOD DEVELOPMENT:

Chromatographic conditions: Column: Thermosil C_{18}Column (100mm x 4.6mm) 5µ. Mobile phase: Phosphate buffer: Methanol P^H 2.5 (35:65 v/v)

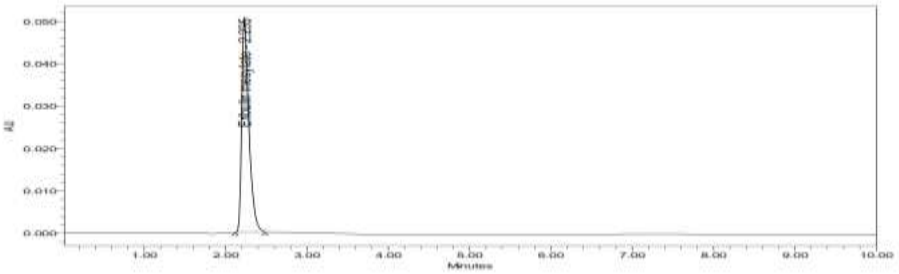
Flow rate : 1ml/ min
Detector wavelength: 254 nm
Injection mode: Autoinjector (vial)
Injection volume: 20µl
Retention time: 2.235

Accuracy

Make half the samples as follows:

The Eribulin Working Reference Standard, accurately weighed at 5 mg, was then dissolved and diluted to volume with mobile phase in a 100 ml volumetric flask to the appropriate concentration. The aforementioned solution was then mixed with 50 ml of mobile phase in a 100 ml standard flask. Pipette 0.5 ml of the aforementioned stock solution into a volumetric flask with a capacity of 10 ml (stock response). Dilute the mark using diluent. The HPLC column was three times injected with the aforementioned solution using the same procedure.

Optimized method



Precision

Standard execution: Exactly 10 mg in weight the material is added to a 100 ml volumetric flask containing the Eribulin working reference standard, which is then dissolved and diluted to the required volume with mobile phase. The aforementioned solution was then mixed with 50 ml of mobile phase in a 100 ml standard flask. (Stock response) Pipette 10 ml of the volumetric flask's capacity with 0.5 ml of the aforementioned stock Solution. Dilute the mark using diluent.

Intermediate Precision (Ruggedness): Ruggedness is the extent to which outcomes of the same sample's analysis may be replicated under a variety of standard test conditions, such as those involving numerous analysts, labs, tools, reagents, assay temperatures, slight changes in the mobile phase, various days, etc (i.e. from laboratory to laboratory, from analyst to analyst).

Standard execution: Weigh 10 mg of the Eribulin Working Reference Standard precisely into a volumetric flask with a capacity of 100 ml. Then, add mobile phase to produce a total volume of 100 ml by transferring 50 ml of the aforementioned solution into a 100 ml standard flask. Pipette 0.5 ml of the aforementioned stock solution into a volumetric flask with a capacity of 10 Ml (stock response). Dilute the mark using diluent.

Procedure: Five repetitions Sample solutions were made in accordance with the test method and administered in accordance with the test protocol.

Robustness: Intentional adjustments were made to the flow rate and mobile phase composition to demonstrate the method's adaptability.

a) **There was a 0.8 to 1.2 millilitre per minute flow rate.**

b) **The organic content of the mobile phase** was changed from 65% to 75% standard solution. The method's actual mobile phase composition as well as several mobile phase compositions were produced and tested on 10 g/ml. In line with the formula, limit of detection (LOD) LODs may be calculated using the SD of the response and S of the calibration curve at values near to the LOD. The standard deviation of the answer may be computed using the standard deviation of the y-intercepts of regression lines.

Results and Discussion:

METHOD VALIDATION

Specificity:

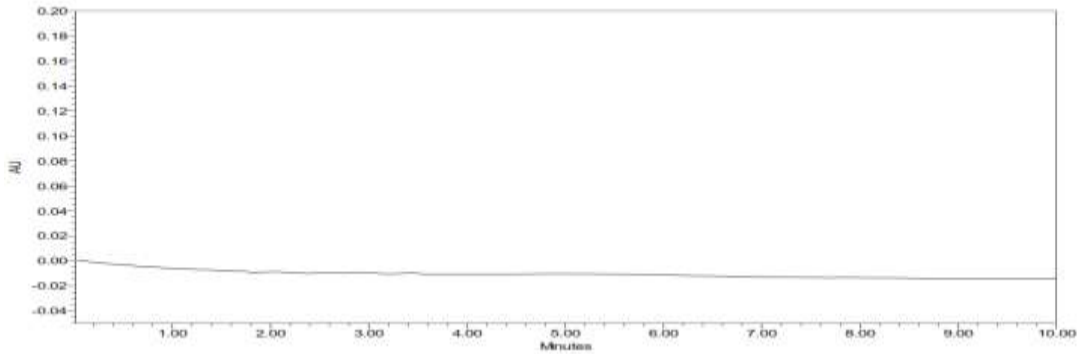


Fig.1: blank (mobile phase preparation)

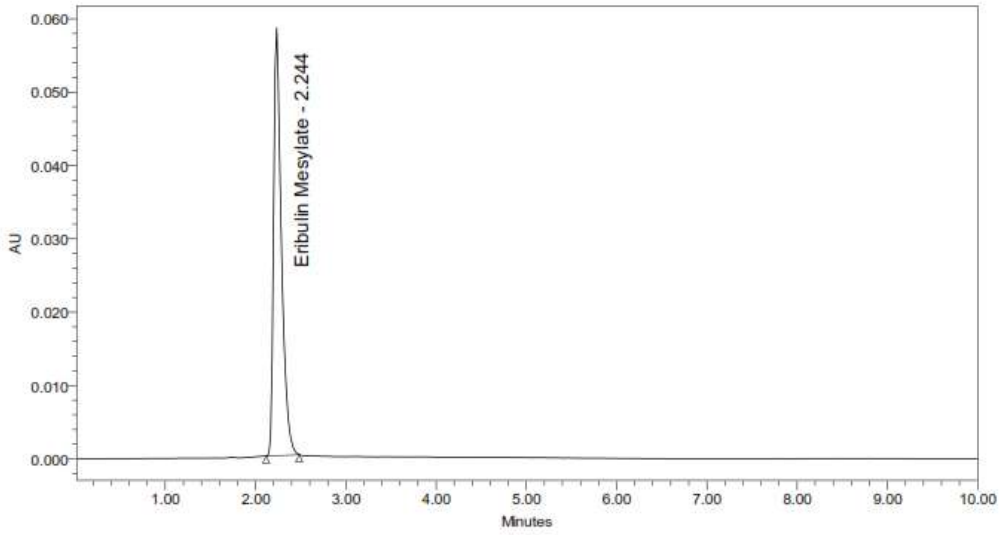


Fig. 2: Sample injection

Linearity of Eribulin mesylate

Sample ID	Eribulin mesylate	
	Concentration	Area
20%	20	1224140
40%	30	1595681
60%	**40***	**1992966**
80%	50	2356546
100%	60	2797214
Correlation Coefficient 0.999		

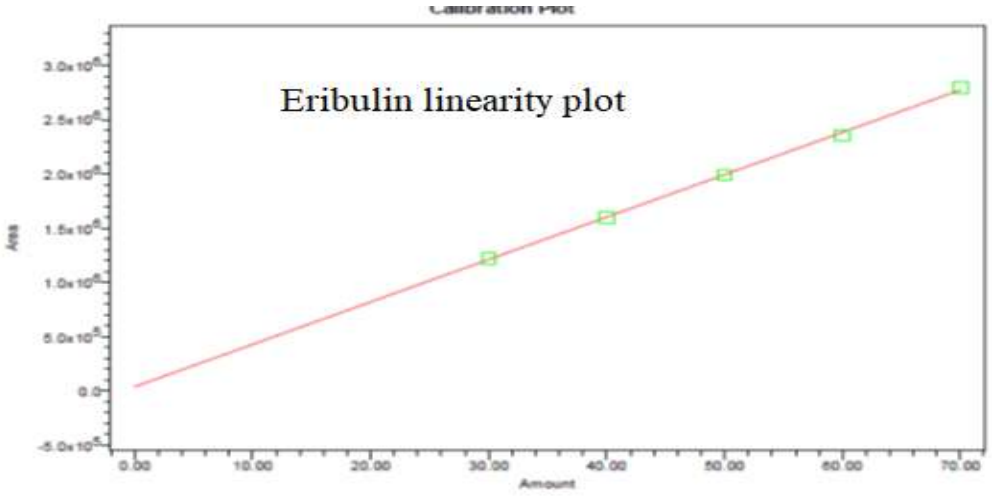


Fig. 3: Calibration curve of Eribulin Mesylate

ACCURACY:

To achieve acceptance requirements, the mean percentage recovery at each spike level must range between NLT 98.0percent to NMT 102.0%. Discussion: The range of the accuracy table's drug recovery rates for other medications and eribulin was 100.01 to 101.39 percent and 99.66 to 101.09 percent, respectively. It seems from this that the process was exact

Recovery Level	Accuracy of Eribulin					Average % Recovery
	Amount taken (mcg/ml)	Area	Average area	Amount recovered (mcg/ml)	Percentage Recovery	
50%	5.05	1011326.25	1017498.5	101.3927	101.3927	
	5.05	1015029				
	5.05	1026141				
100%	10	1986534	1987384.8	100.0106	100.0106	100.599%
	10	1987425				
	10	1988195				
150%	15	2989367	2992493.4	100.3936	100.3936	
	15	2991556				
	15	2996557				

METHOD PRECISION:

S.No	Injection	Peak Name	Rt	Area	Height
1	Injection-1	Eribulin	2.235	2010800	346322
2	Injection-2	Eribulin	2.245	2002956	340800
3	Injection-3	Erinsulin	2.238	2012800	346911
4	Injection-4	Eribulin	2.335	2005243	344089
5	Injection-5	Eribulin	2.234	2011092	345720
Average				2008578.1	
Standard Deviation				4237	
%RSD				0.2	

Acceptance Criteria: % RSD is NMT 2. **Intermediate Precision:**

Injection	Area
Injection-1	2005053
Injection-2	2007362
Injection-3	2007473
Injection-4	2009153
Injection-5	2012800
Average	2008368.1
Standard Deviation	2874.8
%RSD	0.1

Result: The % RSD is NMT 2

Robustness:

Organic phase results for Eribulin

S.No	Change in organic composition in the mobile phase	System suitability results	
		USP Plate Count	USP Tailing
1	-5 %	6498	1.2
2	*+	5026.5	1.3
3	+ 5 %	6471	1.2

LIMIT OF DETECTION: (for Eribulin)

Drug name	Standard deviation(σ)	Slope(s)	LOD(µg)
Eribulin	618048	39092	0.001

The LOD performed for Eribulin was found to be 0.001.

LIMIT OF QUANTITATION

Drug name	Standard deviation(σ)	Slope(s)	LOQ(µg)
Eribulin	618048	39092	0.004

The LOQ performed for Eribulin was found to be 0.004

SUMMARY AND CONCLUSION:

In the present study, an innovative reverse phase HPLC technique was developed for the simultaneous measurement of eribulin in medicinal dosage form. The proposed method's accuracy, precision, ruggedness, linearity, robustness, system applicability, and specificity were all examined in accordance with ICH requirements. Experiment 6 was created to be the most effective trial for developing a way for deliberately changing the chromatographic conditions. The buffer's mobile phase was made up of methanol in a 35:65V/V molar ratio, and orthophosphoric acid was used to bring the pH level down to 2.5. Trerosil C18 (100 mm x 4.6 mm) 5 g served as the column. UV detection was employed at a flow rate of 0.8 ml per minute at 254 nm.

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