An Elsevier Indexed Journal ISSN-2230-7346

Journal of Global Trends in Pharmaceutical Sciences

HIGH PERFORMANCE LIQUID CHROMATOGRAPHIC METHOD FOR THE DETERMINATION OF POMALIDOMIDE IN PHARMACEUTICAL DOSAGE FORMS

Sasidhar Bhimana[1]*, Girija Sankar Guntuku[2]

[1]*Department of Pharmaceutical Biotechnology, Narayana Pharmacy College, Chinthareddypalem-524002, Nellore, A.P., India.*

[2]*Department of Pharmaceutical Biotechnology, College of Pharmaceutical sciences, Andhra University, Visakhapatnam -530003, A.P., India.*

*Corresponding author E-Mail: bhimanasasidhar@gmail.com

ARTICLE INFO

***Key words**:*

Pomalidomide,

liquid Chromatographic method,

Orthophosphoric acid, Correlation coefficient

ABSTRACT

Objective: A simple, rapid, precise and accurate reversed phase high performance liquid chromatographic method has been developed for the determination of Pomalidomide.

Method: In this of 1.0 ml/min and PDA detector method uses a Zobrax Eclipse XDB-C18, 5µm 4.6 X 150mm analytical column, a mobile phase of Acetonitrile: Potassium dihydrogen phosphate buffer pH 2.5 adjusted with orthophosphoric acid in a gradient. The instrumental settings are a flow rate wavelength at 252 nm.

Results: The retention times for Pomalidomide were 4.444 min. The method was validated and shown to be linear. The linearity range for Pomalidomide was 20.24 to 60.72 µg/ml. The Percentage recoveries for Pomalidomide are ranged between 82.90 to 112.3 µg/ml. The correlation coefficient of Pomalidomide was 0.999. The relative standard deviation for six replicates is always less than 2%.

Conclusion: The Statistical analysis proves that the method is suitable for routine analysis of Pomalidomide as a bulk drug and in pharmaceutical formulation.

1. INTRODUCTION:

Pomalidomide is an immune-modulatory antineoplastic agent. The chemical name is (RS)-4- Amino-2-(2,6-dioxo-piperidin-3-yl)-isoindoline-1,3-dione. The empirical formula for pomalidomide is $C_{13}H_{11}N_3O_4$ and the gram molecular weight is 273.24. Pomalidomide is a yellow solid powder. It has limited to low solubility into organic solvents and it has low solubility in all pH solutions (about 0.01 mg/mL) [1].

1.1. **Mechanism of action:** Pomalidomide has direct anti-myeloma tumoricidal activity, immunomodulatory activities and inhibits stromal cell support for multiple myeloma tumour cell growth. Specifically, pomalidomide inhibits proliferation and induces apoptosis of haematopoietic tumour cells. Additionally, pomalidomide inhibits the proliferation of lenalidomide-resistant multiple myeloma cell lines and synergises with dexamethasone in both lenalidomide-sensitive and lenalidomide-resistant cell lines to induce tumour cell apoptosis. Pomalidomide enhances T- cell and natural killer (NK) cell-mediated immunity and inhibits production of pro-inflammatory cytokines (e.g., TNF-α and IL-6) by monocytes. Pomalidomide also inhibits angiogenesis by blocking the migration and adhesion of endothelial cells [2].

Indications and clinical use: Pomalyst® (Pomalidomide) in combination with dexamethasone (Pomalyst® +LD-dex) is indicated for patients with multiple myeloma (MM) for whom both bortezomib and lenalidomide have failed and who have received at least two prior treatment regimens and have demonstrated disease progression on the last regimen. There are no analytical methods that have been reported for the estimation of Pomalidomide in bulk and in pharmaceutical formulations at the time of commencement of research work [3-19]. The present HPLC method deals with new simple, accurate and reliable estimation of Pomalidomide in sterile powder for injections which have been not reported earlier. The other methods reported mainly on the determination of Pomalidomide in plasma, blood samples and biological fluids including tissue homogenates. Such methods may not be suitable for regular/routine analysis for Pomalidomide in pharmaceutical industry because of diversity and complexity in sample matrix. They also have some setbacks and disadvantages of one or the other like requirement of special sample treatment and detection which is not suitable for regular bio-analysis. The determination of Pomalidomide in a Raw Material sample is yet to be found. In addition, stability-indicating methods have been able to be found for the Pomalidomide in pharmaceutical dosage forms. Complete validation parameters were not able to be found in any of the methods reported in the past. Studying the stability of a drug and being able to monitor degradation products aids in the clinical treatments/early product development and shelf life for the drug. They are not suitable for regular/routine analysis in pharmaceutical industry where sample size is more and also less sensitive when compared to HPLC methods. Hence, by considering all these factors, the author has made some humble attempts, hoping to fill this gap, and succeeded in developing analytical methods using HPLC methods.

1.2. Instruments

Quantitative HPLC was performed on the Waters Alliance 2695 Separations Module is a high performance liquid chromatographic system with a quaternary, low-pressure mixing pump and inline vacuum degassing. Flow rates from50 uL/min to 5 mL/min can be generated for use with 2.1 mm ID columns and larger. The auto-sampler has a maximum capacity of 120 vials (12x32, 2-mL) with programmable temperature control from 4 to 40°C. A heated column compartment provides temperatures from 5 degrees above ambient to 65°C. The detector is a photodiode array (model 2996) with a wavelength range of 190-800 nm and sensitivity settings from 0.0001-2.0000 absorbance units.X-Terra RP-C18 Column (250x4.6 mm i.d; particle size 5 µm) was used. The HPLC system was equipped with LC solution software.

2.HPLC Estimation of Pomalidomide

This part of the thesis reports sensitive and precise HPLC method for the determination of drug in bulk and in pharmaceutical formulations. Pomalidomide was found to be completely soluble in acetonitrile and also, Pomalidomide has UV absorption maxima at 254 nm. Hence conventional reverse phase HPLC has been selected for its estimation in pharmaceutical dosage forms.

2.1. Preparation of standard solution

50.6 mg of pomalidomide was accurately weighed and transferred into a 100 ml clean dry volumetric flask, about 70 ml of diluent was added, sonicated it completely and the volume was made up to the mark with the same solvent to give a concentration of 506 µg/ml (Stock solution). Further 5 ml was pipetted out from the above stock solution into a 50ml volumetric flask and diluted up to the mark with diluent to give a concentration of 50.6 µg/ml of pomalidomide. The stock solutions were filtered through a 0.45µ membrane filter paper.

2.2. Preparation of sample solution

10 Tablets of contents were weighed and triturated in glass mortar. The quantity of powder equivalent to 50.6 mg of active ingredient present in pomalidomide was transferred into a 100 ml clean dry volumetric flask, 70 ml of diluent was added to it and was shaken by mechanical stirrer and sonicated for about 30 minutes by shaking at intervals of five minutes each and was diluted up to the mark with diluent to give a concentration of 506 µg/ml and allowed to stand until the residue settles before taking an aliquot for

further dilution (stock solution). 5 ml of upper clear solution was transferred to a 50 ml volumetric flask and diluted with diluent up to the mark to give the respective concentrations as per standard solution. The solution was filtered through m filter before injecting into HPLC system µ0.45.

3. Method validation

The objective of validation of an analytical procedure is to demonstrate that it is suitable for its intended purpose. According to ICH guidelines, the validation parameters were

3.1. System suitability

Sample solution of pomalidomide was injected three times into HPLC system as per test procedure. The system suitability parameters were evaluated from standard Chromatograms obtained, by calculating the % RSD of retention times, tailing factor, theoretical plates and peak areas from three replicate injections.

3.2. Linearity

Preparation of sample stock solution About 50.6 mg of pomalidomide samples were weighed in to 100 ml volumetric flask, it was dissolved with diluent and the volume was made up to the mark with same diluents (506µg/ml of pomalidomide as primary standrard solution). Further 5 ml was pipetted out from the above stock solution into a 50ml volumetric flask and diluted up to the mark with diluent to give a concentration of 50.6 µg/ml of dolutegrevir as secondary standard solution.

Preparation of Level – I (20.24µg/ml of pomalidomide) 4ml of secondary stock solution had taken in 10ml of volumetric flask diluted up to the mark with diluent.

Preparation of Level–II (30.36 µg/ml of pomalidomide) 6ml of secondary stock solution had taken in 10ml of volumetric flask diluted up to the mark with diluent.

Preparation of Level –IIII (40.48 µg/ml of pomalidomide) 8ml of secondary stock solution had taken in 10ml of volumetric flask diluted up to the mark with diluent.

Preparation of Level–IV (50.6 µg/ml of pomalidomide) 10ml of secondary stock solution had taken in 10ml of volumetric flask.

Preparation of Level –V (60.72µg/ml of pomalidomide) 1.2ml of primary stock solution had taken in 10ml of volumetric flask diluted up to the mark with diluent.

3.3. Precision

The precision of the method was checked by repeated injected sample solution of pomalidomide 50.6 micrograms/ml

3.4. Accuracy

Assay was performed in triplicate for various concentrations of pomalidomide equivalent to 80, 100, and 120 % of the standard amount was injected into the HPLC system as per the test procedure.

3.5. Robustness

The robustness of the proposed method was determined by analysis of aliquots from homogenous lots by differing physical parameters like flow rate increase, flow rate decrase and different column which may differ but the responses were still within the specified limits of the assay.

3.5.1 Effect of variation of flow rate

A study was conducted to determine the effect of variation in flow rate. The flow rate was varied at 1.0 ml/min to 1.2 ml/min and to 0.8 ml/min. Standard solution 50.6 ppm (50.6 µg/ml) of pomalidomide was prepared and analysed using the varied flow rates along with method flow rate. The results are summarized on evaluation of the above results, it can be concluded that the variation in flow rate affected the method significantly. Hence it indicates that the method is robust even by change in the flow rate ±10%. The method is robust only in less flow condition. The effect of variation of flow rate was evaluated.

3.6. Limit of detection

The limit of detection was checked by signal to noise ratio. For pomalidomide the prepared solution of 0.0506µg/ml was checked by repeated injected sample solution.

***3.7.* Limit of quantification**

The limit of quantification was checked by signal to noise ratio for pomalidomide. The prepared solution of 0.1518 µg/ml pomalidomide was checked by repeated injected sample solution.

4. Results and discussion

4.1. System suitability

The system suitability tests were carried out on freshly prepared standard stock solution of Pomalidomide. The system was suitable for use, the tailing factors for Pomalidomide were 1.36 and USP theoretical plates were found to be significantly high around 5414.269.

4.2 Precision data

The precision of the method was ascertained separately from the peak area obtained by actual determination of 6 replicas of a fixed amount of drug and formulation. The HPLC systems was set up the described Chromatographic conditions, mentioned as above and follow the system to equilibrate, and then injected the 50 µg/ml concentration of Pomalidomide standard 6 times and recorded the response (peak area). The proposed method was extended to the pharmaceutical dosage forms by injecting the 50 µg/ml of Pomalidomide sample with the formulated sample from (Pomalyst®-2mg, Celgene Corporation, Capsules)contains Pomalidomide of same concentration 6 times and recorded the response (peak area). The percent relative standard deviation and percent range of error (at 0.05 and 0.01 confidence limits) were calculated and presented.

4.3. Linearity data

Aliquots of standard Pomalidomide stock solution were taken in different 10 ml volumetric flasks and diluted up to the mark with the mobile phase such that the final concentrations of Pomalidomide are in the range of 5-60µg/ml. Each of these drug solutions (20 µL) was injected three times into the column, and the peak areas and retention times were recorded. Evaluation was performed with PDA detector at 252 nm and a Calibration graph was obtained by plotting peak area versus concentration of Pomalidomide. The linearity Chromatograms presented.

4.4. Accuracy data

Recovery studies were conducted by analyzing pharmaceutical formulation in the first instance for the active ingredient in the concentration of 80% of the working standard (contains 40 µg/mL of Pomalidomide); 100% of the working standard solution (contains 50 µg/mL of Pomalidomide) and 120% of the working standard solution (contains 60 µg/mL of Pomalidomide) by the proposed method. Each concentration was injected 3 times and the peak area was recorded. Known amounts of pure drug [10% of the working standard solution contains 5 µg/mL of Pomalidomide for 80% of the working standard, for 100% of the working standard, for 120% of the working standard] was then added to each 3 previously analyzed formulation and the total amount of the drug was once again determined by the proposed method (each concentration was again injected 3 times) after keeping the active ingredient concentration within the linearity limits.

4.5. Robustness

A method is robust if it is unaffected by small changes in operating conditions. To determine the robustness of this method, the experimental conditions were deliberately altered at two different levels and retention time and chromatographic response were evaluated. One factor at a time was changed to study the effect. Variation of the mobile phase flow rate was varied by ±10%) and different column had no significant effect on the retention time and chromatographic response of the method, indicating that the method was robust. When the chromatographic conditions were deliberately altered, system suitability results remained within acceptance limits and selectivity for individual substance was not affected. The results of the study prove the robust nature of the method.

4.6. Limit of Detection [LOD] and Limit of Quantification [LOQ]:

The detection limit of the method was investigated by injecting standard solutions Pomalidomide into the HPLC column. By using the signal-to-noise method the peak-to-peak noise around the analyte retention time is measured, and subsequently, the concentration of the analyte that would yield a signal equal to certain value of noise to signal ratio is estimated. A signal-to-noise ratio (S/N) of 3 is generally accepted for estimating LOD and signal-to-noise ratio of 10 is used for estimating LOQ.

Table 1: Structural Features of Pomalidomide

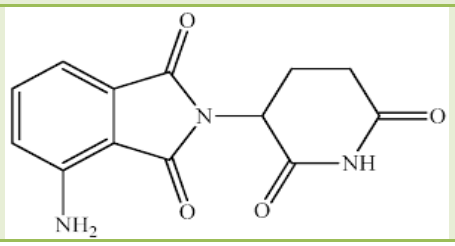
	Chemical Name(s)	Structure
Pomalidomide	4-amino-2-(2,6-dioxo piperidin-3-yl) iso indoline-1,3-dione.	

Table 2: Materials Used

S.NO	Materials	TYPE	BRAND
1	Acetonitrile	HPLC Grade	Merck
2	Water	HPLC Grade	Merck
3	Di-Potassium hydrogen Orthophosphate	AR GRADE	Rankem

Table 3: List of Equipments

S.NO	Instruments	Software	Model	Company
1	HPLC	Empower Software	Waters 515pump,Detector2487	AGILENT
2	UV-Spectrophotometer	UV Analyst	T-60	PG INSTRUMENT
3	Weighing balance	-	XEX 200	SHIMADZU
4	Sonicator	-	SE60US	ENERTECH
5	pH Meter	-	AD102U	ADWA

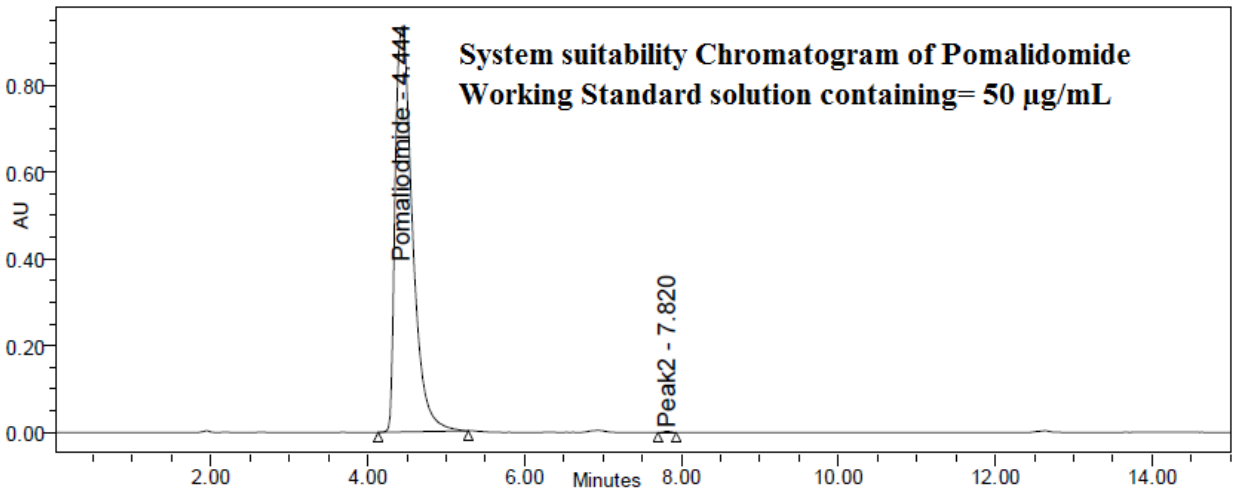


Fig 1: System suitability data

Table 4: System suitability data

Peak #	Ret.Time	Name	Area	Area %	RT time	Theoretical plate#	Tailing Factor	Resolution
1.	4.444	Pomalidomide	13991103	99.86		2295.85	1.46	
2.	7.820	Peak2	17002	0.14	1.76	25654.12	1.15	11.61

Table 5: Precision of Standard drug with statistics

Injection No.	Name of the drug & conc. (50 µg/ml)	Retention time in min.	Peak Area
1	Pomalidomide injection-1	4.44	**14258105**
2	Pomalidomide injection-2	4.43	**14253871**
3	Pomalidomide injection-3	4.41	**14244580**
4	Pomalidomide injection-4	4.43	**14195650**
5	Pomalidomide injection-5	4.43	**14180476**
6	Pomalidomide injection-6	4.45	**14124036**
Mean		4.4	**14209452.9**
% RSD.		0.0	**52726.1**
Std. Deviation		**0.3**	**0.4**

Table 6: Precision study of Sample Solution (Pomolyst®2mg, Capsules**) with statistics**

Injection No.	Name of the drug & conc. (50 µg/ml)	Retention time in min.	Peak Area
1	Pomolyst® injection-1	4.43	**14130740**
2	Pomolyst® injection-2	4.44	**14113317**
3	Pomolyst® injection-3	4.44	**14085496**
4	Pomolyst® injection-4	4.46	**14077114**
5	Pomolyst® injection-5	4.44	**14031450**
6	Pomolyst® injection-6	4.46	**14017572**
Mean		4.4	**14075948.1**
Std. Deviation		0.0	**44449.8**
% RSD		**0.3**	**0.3**

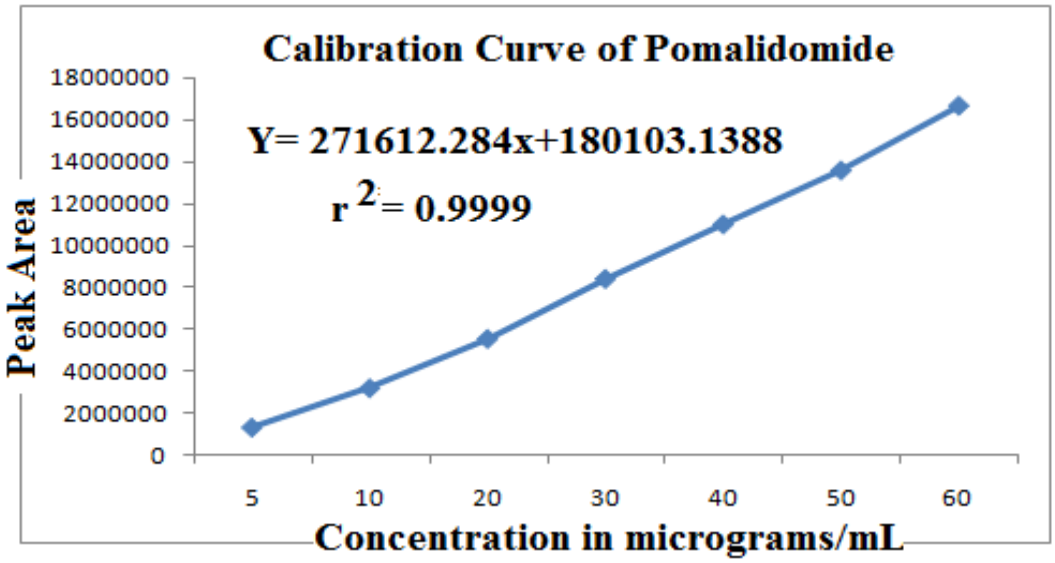


Fig 2: Standard Calibration Curve of Pomalidomide

Table 7: Standard calibration values of Pomalidomide

Concentration of drug (µg/mL)	Retention time	Peak Area
5	4.533	1326319
10	4.511	3199597
20	4.5	5547936
30	4.5	8399016
40	4.4	10992333
50	4.4	13559554
60	4.4	16632608

Table 8: Recovery Peak areas of Pomalidomide by Accuracy studies

S.No	Recovery at 80% dilution level Peak areas		Recovery at 100% dilution level Peak areas		Recovery at 120% dilution level Peak areas	
	Standard	Spiked	Standard	Spiked	Standard	Spiked
1	11085657	12450351	13910908	15361992	17070634	18190333
2	11062914	12461202	13855482	15340595	17079835	18167831
3	11062876	12383217	13835789	15369199	17064215	18143173
Avg	11070482.3	12431590.0	13867393.0	15357262.0	17071561.3	18167112.3
Std.Dev	13141.7	42242.1	38950.2	14877.1	7851.2	23588.2
%RSD	0.1	0.3	0.3	0.1	0.0	0.1
% Recovery	102.20		112.3%		82.90	

Table 9: Robustness study of Pomalidomide Standard solution at 100 % level (50 µg/mL)

Parameter	Peak areas of Pomalidomide in Flow increase study		Peak areas of Pomalidomide in Flow decrease study		Peak areas of Pomalidomide in Variable column Study	
	Run time	**Peak Area**	**Run time**	**Peak Area**	**Run time**	**Peak Area**
Injection-1	4.03	11929105	4.79	14879228	4.41	13341272
Injection-2	4.03	11984866	4.80	14963008	4.43	13371198
Injection-3	4.04	11907976	4.79	14862769	4.44	13326064
Mean	4.0	11940648.9	4.8	14901668.2	4.4	13346177.9
% RSD	0.0	39723.9	0.0	53755.2	0.0	22963.2
Std. Dev	0.1	0.3	0.1	0.4	0.2	0.2

Table 10: Robustness study of Pomolyst®-2 mg capsules solution at 100 % level (50 µg/mL)

Parameter	Peak areas of Pomalidomide in Flow increase study		Peak areas of Pomalidomide in Flow decrease study		Peak areas of Pomalidomide in Variable column Study	
	Run time	**Peak Area**	**Run time**	**Peak Area**	**Run time**	**Peak Area**
Injection-1	4.05	11976336	4.78	14828243	4.42	13317464
Injection-2	4.06	11852294	4.79	14897290	4.42	13270012
Injection-3	4.05	11978216	4.80	14833574	4.41	13284434
Mean	4.1	11935615.3	4.8	14853035.6	4.4	13290636.6
% RSD	0.0	72164.4	0.0	38418.0	0.0	24326.5
Std.Dev	0.1	0.6	0.2	0.3	0.1	0.2

Table 11: LOD and LOQ Data

Level of dilution	Concentraion µg/ml	Area
20%	10.12	2799597
10%	5.06	1326319
5%	2.53	628404
2.00%	1.012	273549
1.00%	0.506	106124
0.50%	0.253	49436
0.20%	0.1012	20008
0.10%	0.0506	10250
0.05%	0.0253	ND
LOD:	0.10%	0.0506
LOQ:	0.30%	0.1518

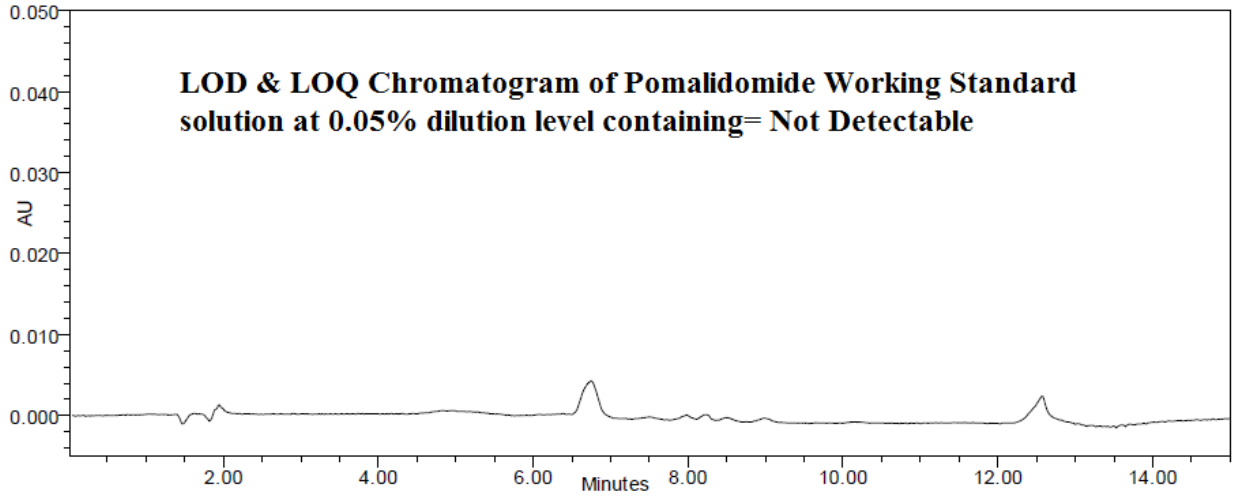


Fig 3: LOD & LOQ Chromatogram of Pomalidone Working Standard solution at 0.05% dilution level

This method is commonly applied to analytical methods that exhibit baseline noise. Chromatograms illustrating the LOD are shown in figure 3. The limit of detection (LOD) and limit of quantification (LOQ) for Pomalidomide were found to be 0.5 µg/ml and 0.1 5 µg/ml respectively.

5.CONCLUSION

High performance liquid chromatography is at present one of the most sophisticated tool of the analysis. A sensitive, accurate and precise HPLC for the estimation of Pomalidomide in bulk drug and in capsules dosage form. From the typical chromatogram of Pomalidomide as shown in fig 3.1.2, it was it found that the retention time was 3.166 min. The contents of the mobile phase were Buffer: Acetonitrile 45: 55 (v/v). Solvent-A (Buffer) is 3.48 gms of Di Potassium hydrogen *ortho*-phosphate (0.03M) in 1000 ml of water and by adjusting the pH to 2.5 with dilute *ortho*-phosphoric acid and Solvent-B is Acetonitrile in a gradient mode of separation was used to resolute the Pomalidomide at a flow rate of 1.0 ml/min and eluents were monitored at 252 nm, was found to be most suitable to obtain a peak well defined and free from tailing. In the present developed HPLC method, the standard and sample preparation required less time and no tedious extraction were involved. A good linear relationship (r^2=0.9998) was observed between the concentration range of 5-60µg/mL. The assay of Pomalidomide in bulk was found to be 99.74%. From the recovery studies it was found that about 108.18 % on average of Pomalidomide was recovered which indicates high accuracy of the method. The absence of additional peaks in the chromatogram indicates non-interference of

the common excipients used in the film coated capsules. This demonstrates that the developed HPLC method is simple, linear, accurate, sensitive and reproducible. Thus, the developed method can be easily used for the routine quality control of bulk and sterile powder for injection dosage form of Pomalidomide within a short analysis time**.** The results obtained on the validation parameters met ICH and USP requirements. It inferred the method found to be simple, accurate, precise and linear. The method was found to be having suitable application in routine laboratory analysis with high degree of accuracy and precision.

Acknowledgement

The authors are thankful to Dr. M. Sreenivasulu, Principal and Mr. Vinay Kumar, Management of Narayana Pharmacy college, Nellore, Andhra Pradesh, for providing suitable environment for successful completion of work.

REFERENCES

1. Corral LG, Haslett PA, Muller GW, Chen R, Wong LM, Ocampo CJ, et al. Journal of immunology. 1999; **163(1):** 380–386.
2. Muller GW, Chen R, Huang SY, Corral LG, Wong LM, Patterson RT,et al. Amino-substituted thalidomide analogs: potent inhibitors of TNF-alpha production. Bioorganic and medicinal chemistry letters. 1999; 9(11); 9: 1625–1630.
3. Crane E, List A. Lenalidomide: an immunomodulatory drug. Future oncology. 2005;**1(15)**: 575–583.
4. Zhu D, Corral LG, Fleming YW, Stein B. Immunomodulatory drugs Revlimid (lenalidomide) and CC-4047 induce apoptosis of both hematological and solid tumor cells through NK cell activation. Cancer immunology, immunotherapy: CII. 2008;**57(12)**: 1849–1859.
5. Streetly MJ, Gyertson K, Daniel Y, Zeldis JB, Kazmi M, Schey SA. Alternate day pomalidomide retains anti-myeloma effect with reduced adverse events and evidence of in vivo immunomodulation. British journal of haematology.2008; **141(1)**:41–51.
6. Cooney MM, Nock C, Bokar J, Krishnamurthi S, Gibbons J, Rodal MB, Ness A, et al. Phase I trial of pomalidomide given for patients with advanced solid tumors. Cancer chemotherapy and pharmacology. 2012 Nov;**70 (5)**:755–761.
7. Gertz MA. Pomalidomide and myeloma meningitis. Leukemia& lymphoma. 2013;**54 (4):**681–682.
8. Weingärtner S, Zerr P, Tomcik M, Palumbo-Zerr K, Distler A, Dees C, Beyer C, et al. Pomalidomide is effective for prevention and treatment of experimental skin fibrosis. Annals of the rheumatic diseases. 2012 Nov ;**71(11)**:1895–1899.
9. Mussetti A, Dalto S, Montefusco V. Effective treatment of pomalidomide in central nervous system myelmatosis. Leukemia& lymphoma. 2013 Apr ;54 (4):864–866.
10. Dispenzieri A, Buadi F, Laumann K, LaPlant B, Hayman SR, Kumar SK, et al. Activity of pomalidomide in patients with immunoglobulin light-chain amyloidosis. Blood. 2012 Jun ; **119 (23)**:5397–5404.
11. Zhu YX, Kortuem KM, Stewart AK. Molecular mechanism of action of immune-modulatory drugs thalidomide, lenalidomide and pomalidomide in multiple myeloma. Leukemia& lymphoma. 2013 Apr ; 54 (4):683–687.
12. Escoubet-Lozach L, Lin IL, Jensen-Pergakes K, Brady HA, Gandhi AK, Schafer PH et al. Pomalidomide and lenalidomide induce p21 WAF-1 expression in both lymphoma and multiple myeloma through a LSD1-mediated epigenetic mechanism. Cancer research. 2009 Sep;69 (18):7347–7356.
13. Moutouh-de Parseval LA, Verhelle D, Glezer E, Jensen-Pergakes K, Ferguson GD, Corral LG. Pomalidomide and lenalidomide regulate erythropoiesis and fetal hemoglobin production in human CD34+ cells. The Journal of clinical

investigation. 2008 Jan;118 (1):248–258.

14. Hoffmann M, Kasserra C, Reyes J, Schafer P, Kosek J, Capone L,et al. Absorption, metabolism and excretion of [14C]pomalidomide in humans following oral administration,. Absorption, metabolism and excretion of [14C]pomalidomide in humans following oral administration. Cancer chemotherapy and pharmacology. 2013;**71 (2)**:489–501.
15. Begna KH, Pardanani A, Mesa R, Litzow MR, Hogan WJ, Hanson CA, et al. Long-term outcome of pomalidomide therapy in myelofibrosis. American journal of hematology. 2012 Jan;**87(1):**66–68.
16. Infante JR, Jones SF, Bendell JC, Spigel DR, Yardley DA, Weekes CD, et al. A phase I, dose-escalation study of pomalidomide (CC-4047) in combination with gemcitabine in metastatic pancreas cancer.3rd European journal of cancer. 2011Jan ;47(2):199–205.
17. Mesa RA, Pardanani AD, Hussein K, Wu W, Schwager S, Litzow MR, et al. Phase1/-2 study of Pomalidomide in myelofibrosis. American journal of hematology. 2010 Feb;**85(2)**:129–130.
18. Begna KH, Mesa RA, Pardanani A, Hogan WJ, Litzow MR, McClure RF, et al. A phase-2 trial of low-dose pomalidomide in myelofibrosis. Leukemia: official journal of the Leukemia Society of America, Leukemia Research Fund, UK. 2011 Feb; **25 (2)**:301–304.
19. Schey S, Ramasamy K.Pomalidomide therapy for myeloma. Expert opinion on investigational drugs. 2011May; 20 **(5)**:691–700.