WORLD JOURNAL OF PHARMACEUTICAL RESEARCH
SJIF Impact Factor 7.523
Volume 6, Issue 3, 539-564. Research Article ISSN 2277– 7105

QUANTITATIVE DETERMINATION AND VALIDATION OF OLMESARTAN MEDOXOMIL IN PHARMACEUTICAL USING QUANTITATIVE NUCLEAR MAGNETIC RESONANCE SPECTROSCOPY

Jeetendra Kumar*[1], Rajnish Kumar[2] and Partha Mukharjee[3]

[1]Department of Pharmaceutical Chemistry, Noida Institute of Engineering & Technology Greater Noida-201306, U.P, India.

[2]Department of Pharmaceutical Chemistry, Noida Institute of Engineering & Technology Greater Noida-201306, U.P, India.

[3]Senior Research Scientist Jubilant Chemsys Limited, Noida U.P, India.

Article Received on
04 Jan. 2017,

Revised on 24 Jan. 2017,
Accepted on 14 Feb. 2017

DOI: 10.20959/wjpr20173-6874

***Corresponding Author**
Jeetendra Kumar
Department of Pharmaceutical Chemistry, Noida Institute of Engineering & Technology Greater Noida-201306, U.P, India.

1. ABSTRACT

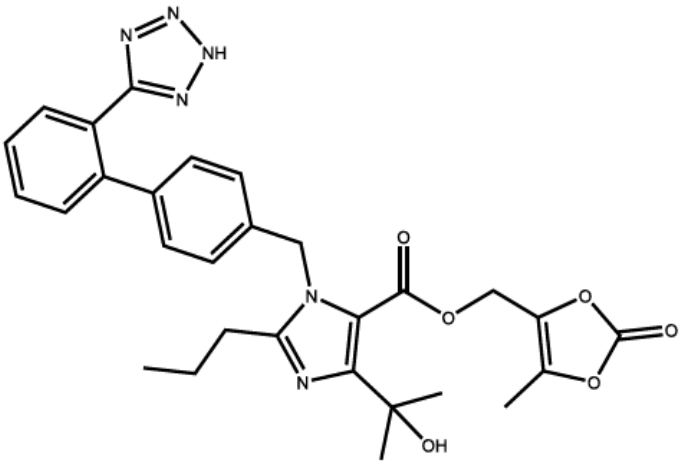
Rapid, specific and accurate Proton nuclear magnetic resonance spectroscopy (^{1}H-NMR) method was developed to determine Olmesartan medoxomil drug in pharmaceutical tablet formulation. The method was based on quantitative NMR spectroscopy (qNMR) using Maleic acid as an internal standard and deuterated dimethylsulfoxide (DMSO- D_6) as an NMR solvent. For the quantification of the drug, the ^{1}H-NMR signals at 2.75 ppm and 6.25 ppm corresponding to the analyte proton of Olmesartan medoxomil drug and Maleic acid internal reference standard (IS) respectively were used. The method was validated for the parameters of specificity and selectivity, precision and intermediate precision, linearity, accuracy and robustness. The linearity of the calibration curve for analyte in the desired concentration range is good (R2 =0.9992). The method was accurate and precise. The advantage of the method is that no reference standard of analyte drug is required for quantification. The method is non-destructive and can be applied for quantification of Olmesartan medoxomil in commercial formulation products. The method was validated specificity, precision, linearity, accuracy and robustness. The linearity of Olmesartan- medoxomil was in the range and correlation coefficient was found to be 0.9962. The recovery was found in the range. The developed

method was validated as per International Conference on Harmonization guidelines (ICH) with respect to specificity, linearity, accuracy, precision, solution stability and robustness.

2. KEYWORDS: Olmesartan Medoxomil, NMR, new method development, validation, QNMR.

3. INTRODUCTION

Olmesartan Medoxomil is a typical antihypertensive drug used in the treatment of high blood pressure likeproblems. Olmesartan Medoxomil has the chemical name (5-methyl-2-oxo-2H-1,3-dioxol-4-yl)methyl,4-(2-hydroxypropan-2-yl)-2-propyl-1-({4-[2-(2H-1,2,3,4-tetrazol-5-yl)phenyl] phenyl}methyl)-1H-imidazole-5-carboxylate (Figure 1). It has angiotensin II receptor antagonist like property.[1] The Olmesartan Medoxomil drug is mainly used for hypertension in countries like Japan and US. The Medoxomil moiety, which is enclosed with this drug, has endogenous ester moietyresponsible for releasing metabolites in the body. Olmesartan Medoxomil has a favorable safety andefficacy profile, with blood pressure-lowering effects comparable to those of other angiotensin receptorblockers (i.e. Losartan, Valsartan, Irbesartan).[2] This drug was developed by Sankyo in 1995, and is available in the market with the trade name of Benicar, Olmetec and Olmesar. High Performance Thin Layer Chromatography (HPTLC) has been used to quantify[Olmesartan Medoxomil in many cases. The earlier reported study of this drug was mainly performed by RPHPLC methods on long columns with higher particle size, which were more time consuming. Even though the method was using complex mobile phase mixture with high flow rates, the analysis was lacking sensitivity and peak symmetry. The purpose of the present study is to develop a simple, sensitive, accurate, precise, rugged and time saving method for the determination of Olmesartan Medoxomil in formulated product. The target is attained by selecting more advance technique of Waters Acquity UPLC, which gives more accurate result in shorter run time. The method development is done by optimizing the experimental conditions using mass compatible volatile buffer i.e. Ammonium Acetate, on a shorter column having 1.7µm particle size. The developed method has been validated by following several parameters as mentioned in ICH guideline i.e. linearity, specificity, accuracy, precision, robustness, ruggedness, stability. The pure Active Pharmaceutical Ingredient (API), used in this project, is manufactured by GLENMARK Company and obtained from Jubilant Life Science Limited with a COA (Certificate of Analysis). The Tablet used was OLMESAR, manufactured by Macleods Pharmaceutical Ltd.



Chemical Formula: $C_{29}H_{30}N_6O_6$

Exact mass: 558.54

Figure 1. Structure of Olmesartan Medoxomil.

4. MATERIAL AND METHOD

4.1 STANDARD DETAILS FOR NMR

Table 4.1 Standard details

Standard Name	Manufacturer		Purity	Storage condition
Olmesartan Medoxomil	Taj Pharmaceuticals Ltd.		99 %	Stored in a well closed container

4.2 SAMPLE DETAILS FOR NMR

The drug substance used for the validation purpose was manufactured by Eris Life Sciences Pharmaceutical Ltd.

TABLE 4.2 Sample details

Sample name	Batch number	Date of manufacture
Olmin	OLM2022B	APRIL 2015

4.3REAGENTS AND SOLVENTS

Table 4.3 Solvent details

S.No	Name	Manufacturer	Grade	Batch no.
1	DMSO d-6	Sigma Aldrich	NMR	LOT#MKBR3576V
2	D2O	Sigma Aldrich	NMR	LOT#S2BC1895V
3	CDCl3	Sigma Aldrich	NMR	D007H-LOTM0201

4.4 INSTRUMENT DETAILS

Instruments used for the validation purpose were:

Table 4.5 instrument details

S. No.	Instrument	Manufactured by	Instrument ID
1	Brukeravance II(400)	Bruker	JCL/ANAL/NMR/02&03
2	Balance	Mettler Toledo (XS 205 dual range)	JCL/ANAL/BALANCE/03
3	Sonicator	Ultrasonicator	JCL/ANAL/US/01

4.5 TO DEVELOP A NEW ANALYTICAL METHOD FOR DRUG FOLLOWING STEPS ARE COVERED

4.5.1 Procurement of drug and sample

- **Drug details**

A well-characterized working standard of Olmesartan Medoxomil with certificate of analysis was used throughout the validation study.

Table 4.6 Drug Details

Standard name	Manufacturer	Purity	Storage condition
Olmesartan-Medoxomil	Taj Pharmaceuticals Ltd.	98.%	Stored in a well closed container

- **Sample details**

The drug substance used for the validation purpose was SUN PHARMA LTD. Olmesartan medoxomil tablet. The batch number and other relevant details of the drug substance to be used are mentioned below.

Table 4.7 Sample Details

Sample name	Batch number	Date of manufacture
Olmin	OLM2022B	APRIL 2015

5. RESULTS AND DISCUSSION

5.1 VALIDATION PARAMETERS FOR THE ASSAY OF OLMESARTAN MEDOXOMIL BY NMR METHOD

Validation is a documented program that provides a high degree of assurance that a facility or operation will consistently produce product meeting a predetermined specifications. According to ICH, it is establishing documented evidence, which provides a high degree assurance that a specific process will consistently produce a product meeting its determined specifications and quality attributes.

The assay procedure was validated for the following parameters.

- Specificity
- Linearity
- Precision
- Intermediate precision
- Accuracy
- Robustness

a) Changing the no. of scans (64±16).

b) Changing the IS (Internal Standard) amount 20% variation(10±2).

5.2 METHOD VALIDATION OF OLMESARTAN MEDOXOMIL

5.2.1 Specificity

Specificity study was performed by analyzing the diluents (DMSO-d6), placebo solution preparation, Olmesartan medoxomil standard preparation, maleic acid IS preparation and sample(tablet) preparation. It was concluded that there was no interference at the signals obtained at 2.91 ppm and 6.25 ppm for analyte proton & IS respectively due to diluents & placebo. Also the signals of the analyte proton and IS were well separated from each other in standard and sample preparations.

Preparation of sample

Olmesartan medoxomil standard preparation for specificity

10.32 mg Olmesartan medoxomil standard was weighed accurately and transferred to stoppperd tube and 0.6 ml DMSO-d_6 was added solution was mixed till complete dissolution.

Marketd preparation for specificity

Marketed drug crushed and thoroughly ground in to fine powder. 24.42 mg marketed drug transferred to stopred tube. Then 0.6 ml of stock solution of maleic acid was added. Solution was thoroughly mixed till complete dissoiution and supernatant was taken.

Placebo solution preparation for specificity

Accurtaly weighed 13.50mg of placebo and transferred (mixed of excipient without drug) to stoppered tubeand 0.6 ml of DMSO was added. Solution was throuhgly mixed till the complete dissolution and supernatant was tsaken for analysis.

Maleic acid (IS) preparation for specificity

10 mg maleic acid in 0.6 ml DMSO- d_6 used.

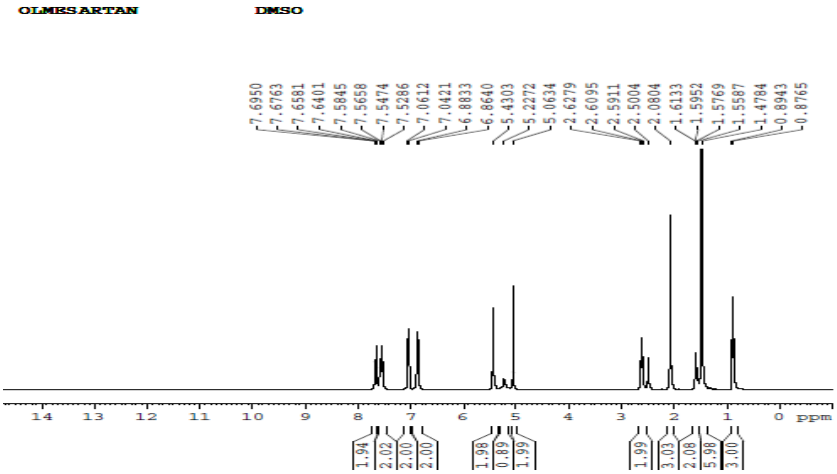


Fig.5.1 Olmesarstan standard preparation

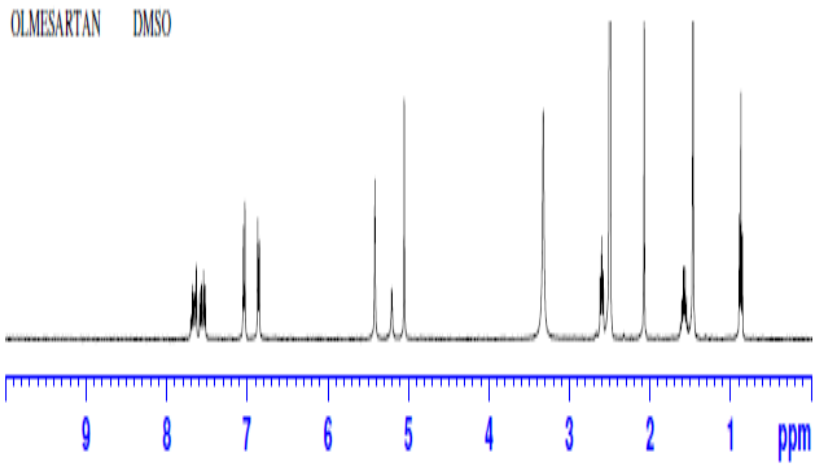


Fig.5.2 Marketed preparation

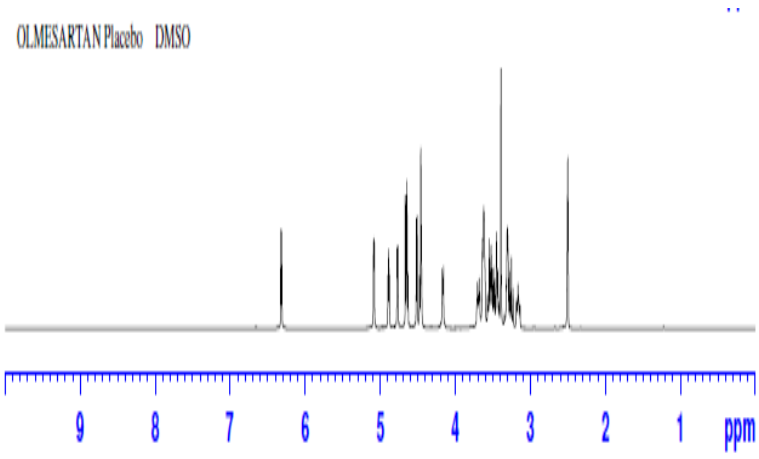


Fig.5.3 Placebo solution Preparation

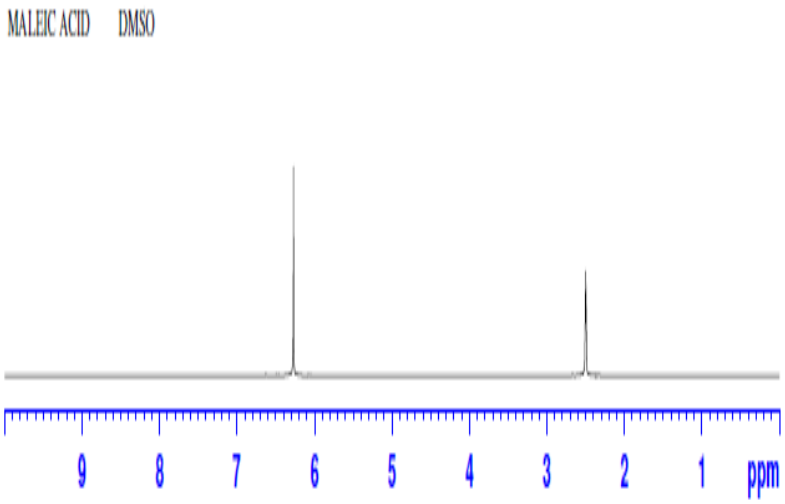


Fig5.4 Maleic acid (IS) Preparation

5.2.2 Linearity

Q-NMR as a method itself is liner because the intensity of the response signal is directly proportional to the amount of nuclei contributing to this signal. Linearity was cheeked by preparing standard solution at 6 different conc. Levels ranging from 70% to 170%, according to content of analyte in sample. Linearity curve was drawn for taken drug amount(in mg) vs. found drug amount(im mg). The equation for curve was y=1.012x-0.128. the correlation coefficient was found 0.999, indicating good linearty.

Calculation

$$\%\text{Assay} = \frac{I(A) \times M.W(A) \times No.ofHs(B) \times W(B) \times A(B)}{No.\ of\ Hs\ (A) \times W(A) \times I(B) \times M.W.(B)}$$

Where,

I (A) = integration value of analyte proton,

M.W. (A) = molecular weight of standard drug,

No. of Hs = no. of highest proton of internal standard (IS),

W (B) = weight of IS,

A (B) = Purity,

No. of Hs (A) = no. of highest proton of standard,

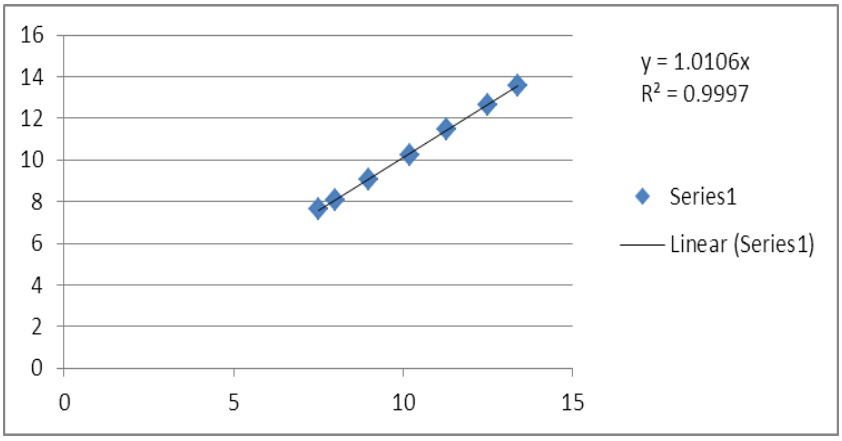
W (A) = weight of standard,

I (B) = integration value of IS,

M.W. (B) = molecular weight of IS.

Table:-5.1 Tabular representation of the linearity parameter.

No. of reading	Internal standard (B)*		Compound of interest (A)#		%age	Amount Obtained
	Weight (mg)	Norm. Integration	Weight (mg)	Norm. Integration	Recovery	Weight (mg)
1st	10.00	2.00	7.5	0.32	101.65	7.62
2nd	10.00	2.00	8.0	0.34	101.25	8.1
3rd	10.00	2.00	9.0	0.38	100.59	9.05
4th	10.00	2.00	10.20	0.43	100.43	10.24
5th	10.00	2.00	11.30	0.48	101.20	11.44
6th	10.00	2.00	12.50	0.53	101.01	12.63
7th	10.00	2.00	13.4	0.57	101.34	13.58



Graph:-1 Graphical representation of the linearity

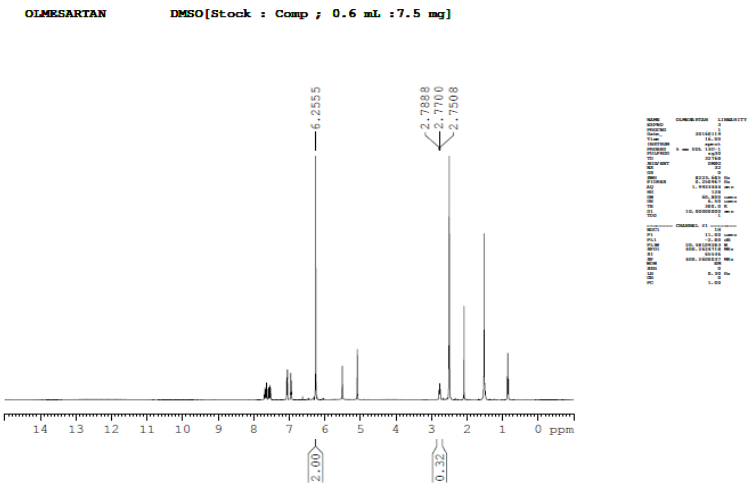


Fig. 5.5.1 Spectra of linearity 7.5 mg std+ 0.6 ml stock

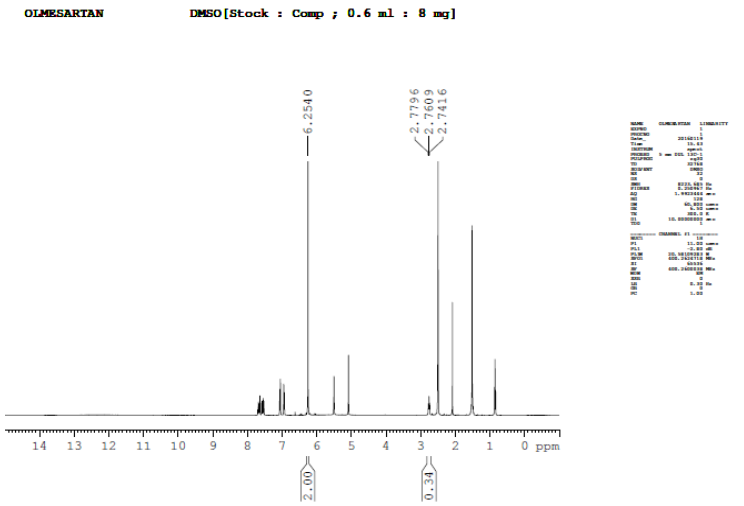


Fig. 5.5.2 Spectra of linearity 8.0 mg std+ 0.6 ml stock

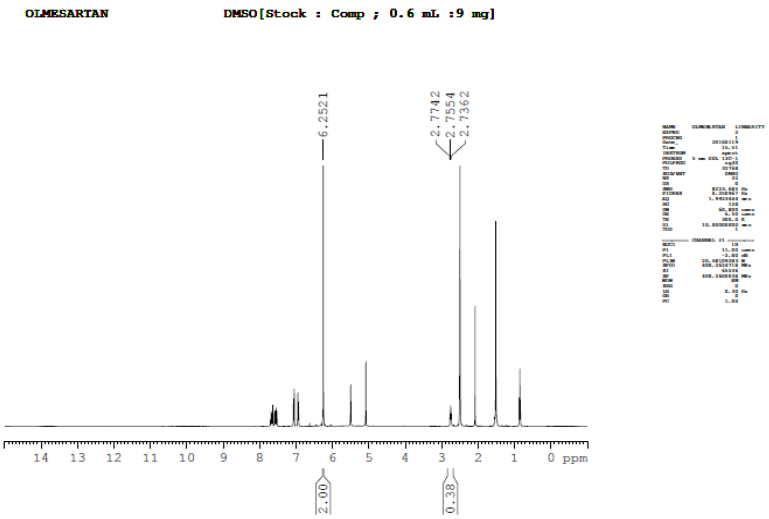


Fig. 5.5.3 Spectra of linearity 9.0 mg std+ 0.6 ml stock

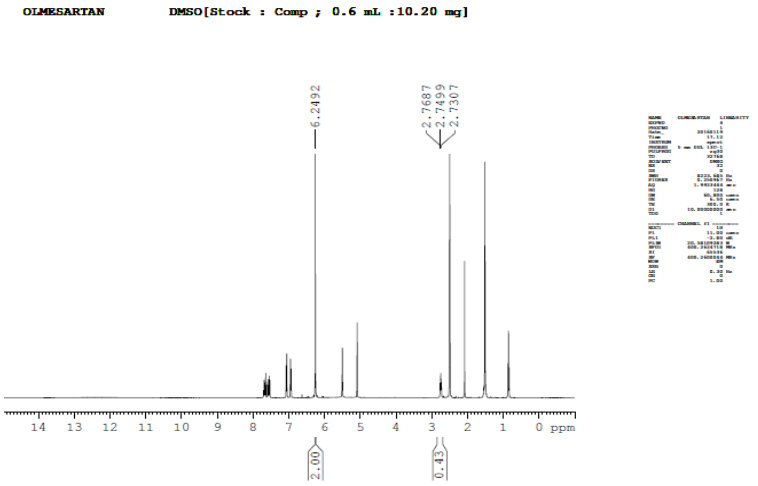


Fig.5.5.4 Spectra of linearity 10.20mg std+ 0.6 ml stock

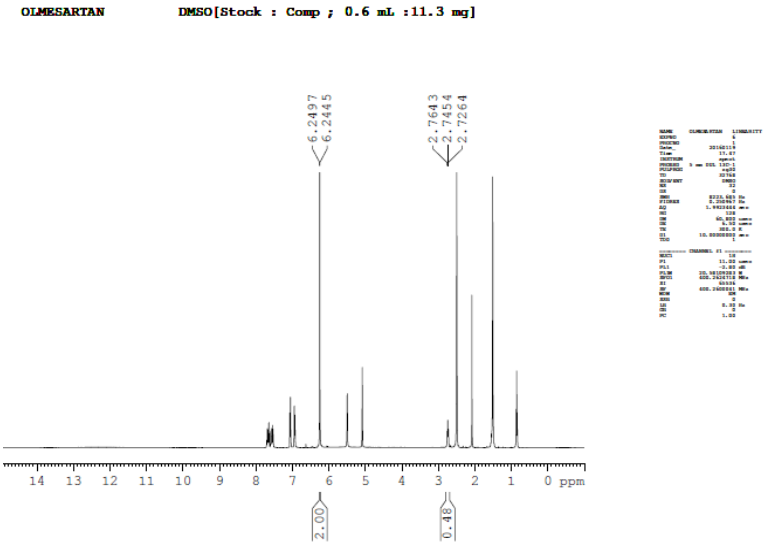


Fig.5.5.5 Spectra of linearity 11.3 mg std+ 0.6 ml stock

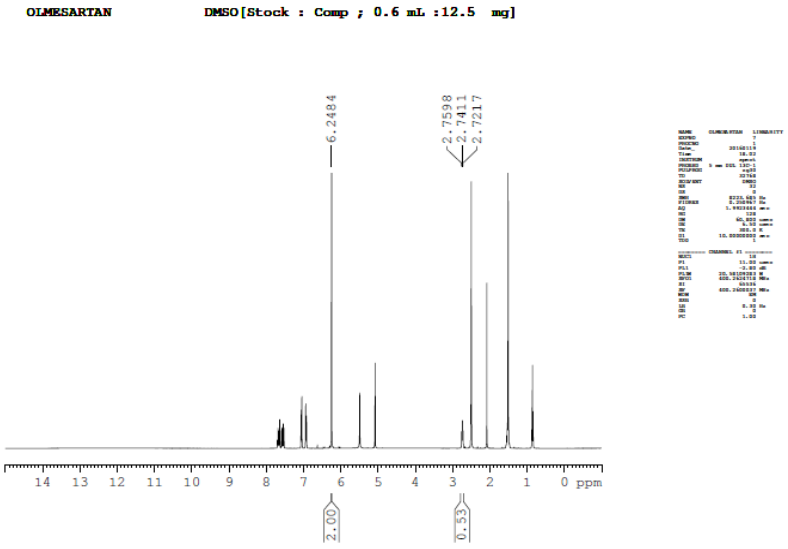


Fig.5.5.6 Spectra of linearity 12.5 mg std+ 0.6 ml stock

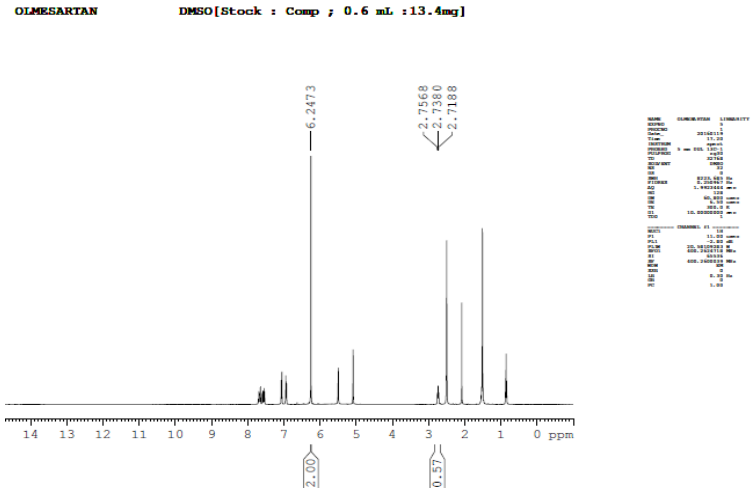


Fig.5.5.7 Spectra of linearity 13.4 mg std+ 0.6 ml stock

5.2.3 PRECISION

The precision of an analytical method expresses the closeness's of agreement between a series of measurements obtained from multiple sampling of the same homogenous sample. According to the ICH guidelines the precision will be acquired by six repeated determinations (n=6). The precision was assessed by six separate sample preparations. Calculated the content of drug in % assay for each preparation and statistical results were tabulated.

Objective: Quantitative analysis of given compound **OLMESARTAN** BY NMR for precision.

Experiment: ^{1}H NMR, Solvent DMSO-d6.

OBSERVATIONS

Table:-5.2 Tabular representation of the precision parameter

No. of reading	Internal standard (B)*		Compound of interest (A)#		%age	Amount obtained
	Weight (mg)	Norm. Integration	Weight (mg)	Norm. Integration	Recovery	Weight (mg)
1st	10.00	2.00	10.90	0.46	100.54	10.96
2nd	10.00	2.00	10.84	0.46	101.09	10.96
3rd	10.00	2.00	10.32	0.44	101.57	10.48
4th	10.00	2.00	10.65	0.45	101.28	10.48
5th	10.00	2.00	10.44	0.44	100.41	10.48
6th	10.00	2.00	10.13	0.43	101.13	10.24

Constant:- 2382.36

No. of Hs (I.S) =2

No. of Hs (COI) = 2

* I.S. is Maleic acid, M.W. = 116.06, Purity (A(B)= 99%

#COI is **OLMESARTAN**, M.W. =558.58.

Formula Used

$$Assay\ of\ the\ sample = \frac{I(A)\times MW(A)\times No.ofHs(B)\times W(B)\times A(B)}{No.ofHs(A)\times W(A)\times I(B)\times MW(B)}$$

Table 5.2.1 Precision

Taken drug in mg	Found drug in mg	%Assay(As such)
10.90	10.96	100.54
10.84	10.96	101.09
10.32	10.48	101.57
10.65	10.48	101.28
10.44	10.48	100.41
10.13	10.24	100.13
	Mean	**101.00**
	SD	**0.31**
	%RSD	**0.30**

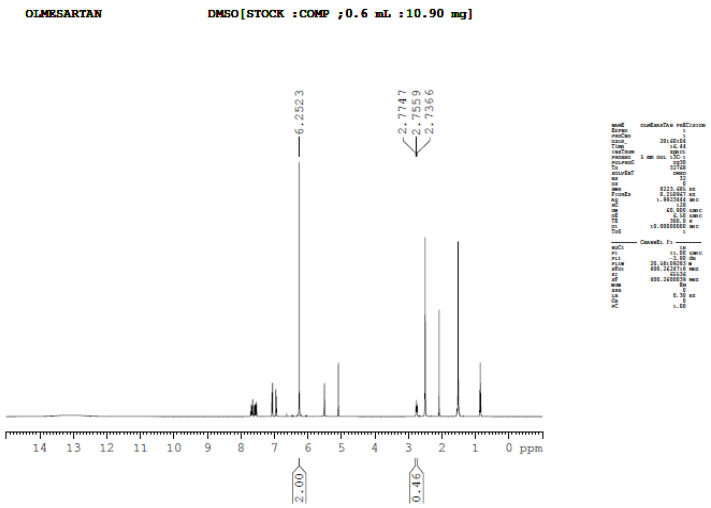


Fig.5.6.1 Precision 10.90 mg Std + 0.6 ml stock

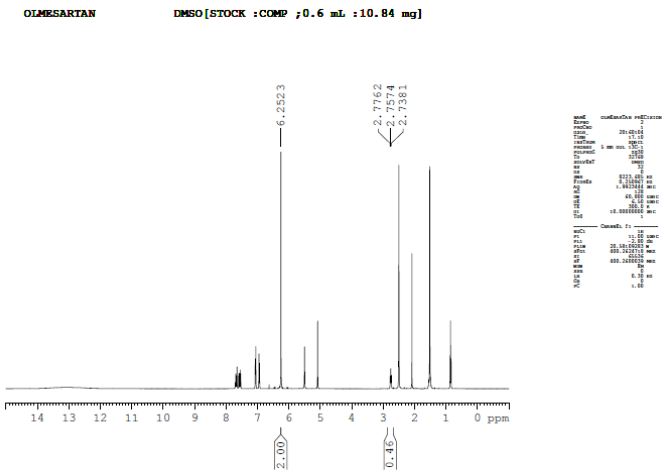


Fig.5.6.2 Precision 10.84 mg Std + 0.6 ml stock

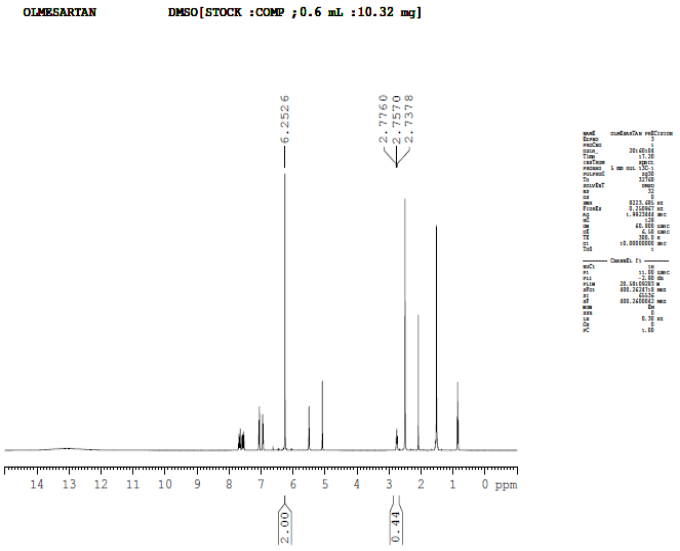


Fig.5.6.3 Precision 10.32 mg Std + 0.6 ml stock

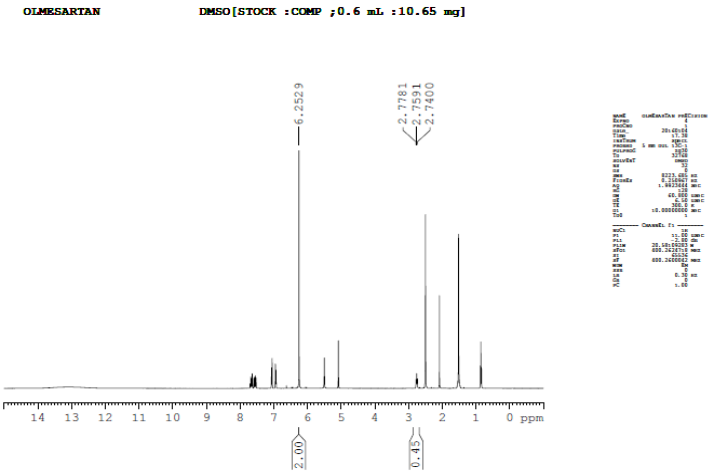


Fig.5.6.4 Precision 10.65 mg Std + 0.6 ml stock

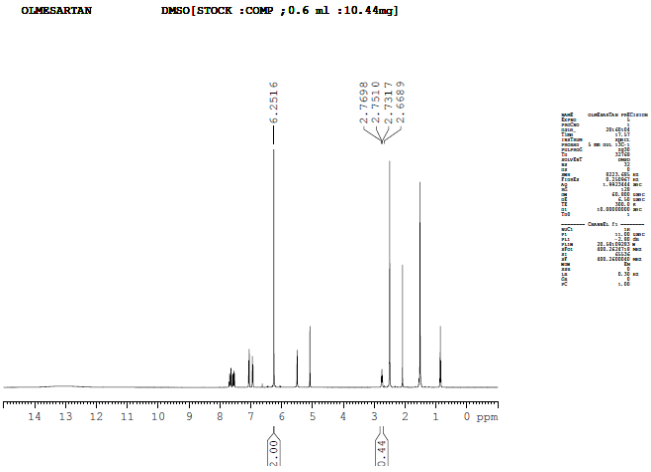


Fig.5.6.5 Precision 10.44 mg Std + 0.6 ml stock

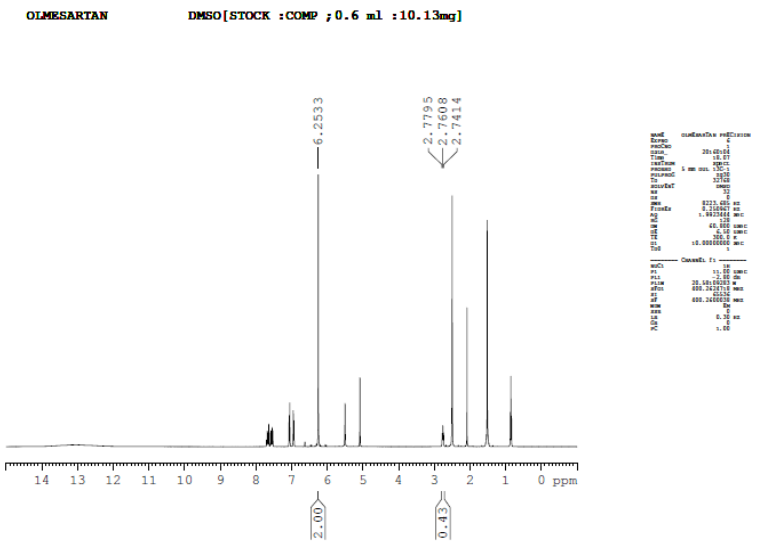


Fig.5.6.6 Precision 10.13 mg Std + 0.6 ml stock

5.2.4 INTERMEDIATE PRECISION

The intermediate precision will be evaluated by a different analyst on different day and/or different NMR probe and/or a different NMR spectrometer with a different magnetic field strength. Integration of peaks as well as phase and baseline correction is the most subjective parts of the method. Six different sample preparations were prepared and analyzed on different day. The average of six analyses, standard deviation(SD) and RSD values are documented in table.

Objective: Quantitative analysis of given compound **OLMESARTAN** by NMR for Intermediate precision.

Experiment: ^{1}H NMR, Solvent DMSO.

OBSERVATIONS

Table:-5.3 Tabular representation of The intermediate precision parameter

No. of reading	Internal standard (B)*		Compound of interest (A)#		%age	Amount obtained
	Weight (mg)	Norm. Integration	Weight (mg)	Norm. Integration	Recovery	Weight (mg)
1st	10.00	2.00	10.80	0.45	100.06	10.81
2nd	10.00	2.00	10.60	0.45	101.14	10.72
3rd	10.00	2.00	10.50	0.45	102.10	10.72
4th	10.00	2.00	10.20	0.43	100.43	10.24
5th	10.00	2.00	10.70	0.45	100.19	10.72
6th	10.00	2.00	10.10	0.43	100.43	10.14

Constant:- 2382.36

No. of Hs (I.S) =2

No. of Hs (COI) = 2

* I.S. is Maleic acid, M.W. = 116.06, Purity (A(B)= 99%

#COI is **OLMESARTAN**, M.W. =558.58.

Formula Used

$$Assay\ of\ the\ sample = \frac{I(A)\times MW(A)\times No.ofHs(B)\times W(B)\times A(B)}{No.ofHs(A)\times W(A)\times I(B)\times MW(B)}$$

Table:-5.3.1 intermediate precision

Taken drug in mg	Found drug in mg	%Assay(As such)
10.80	10.81	100.06
10.60	10.72	101.14
10.50	10.72	102.10
10.20	10.24	100.43
10.70	10.72	100.19
10.10	10.14	100.43
	Mean	100.7
	SD	1.30
	%RSD	1.29

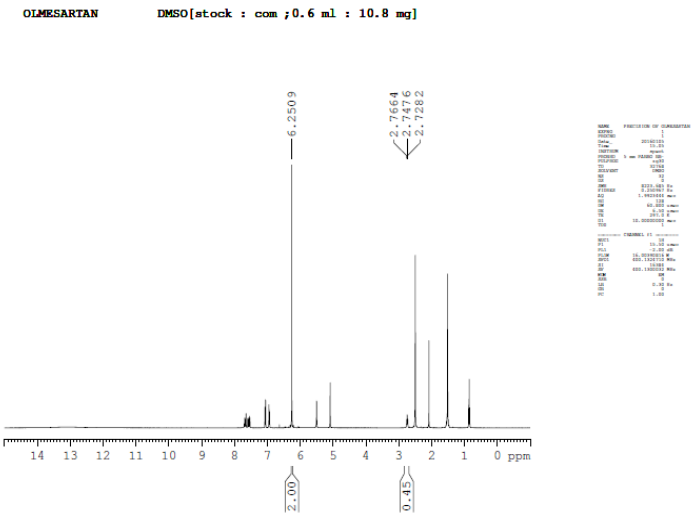


Fig.5.7.1 Intermediate Precision 10.8 mg + 0.6 ml stock

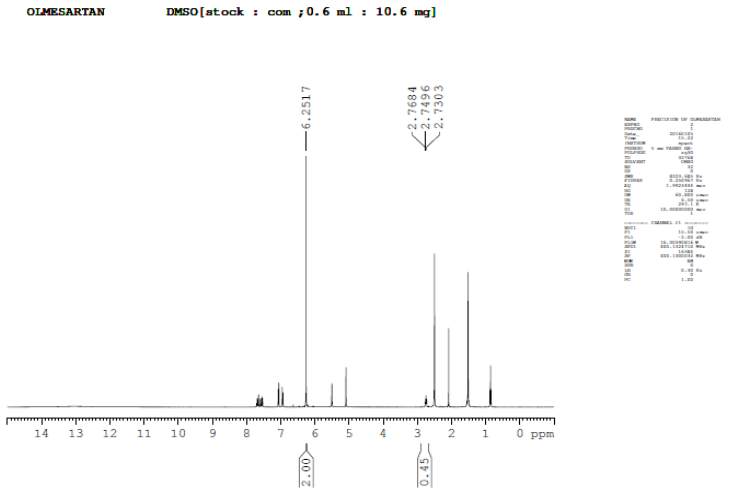


Fig.5.7.2 Intermediate Precision 10.6 mg + 0.6 ml stock

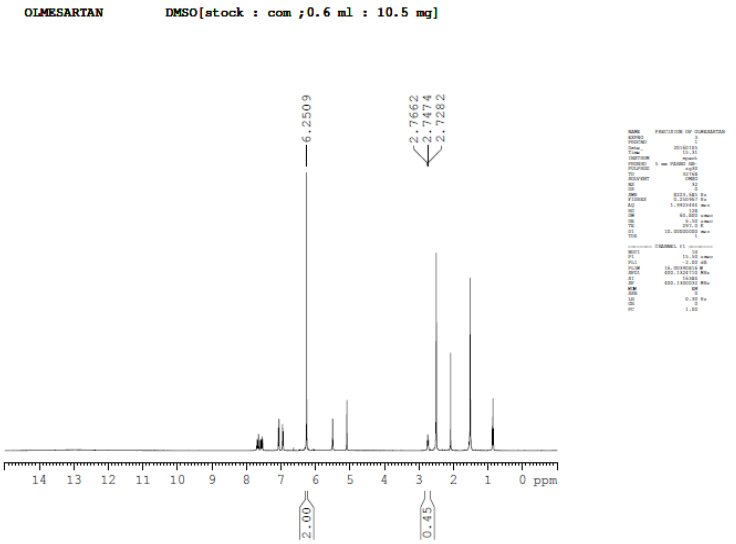


Fig.5.7.3 Intermediate Precision 10.5 mg + 0.6 ml stock

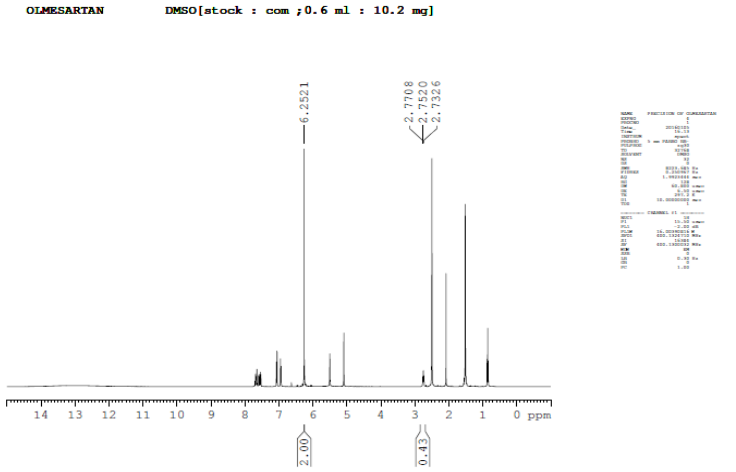


Fig.5.7.4 Intermediate Precision 10.2 mg + 0.6 ml stock

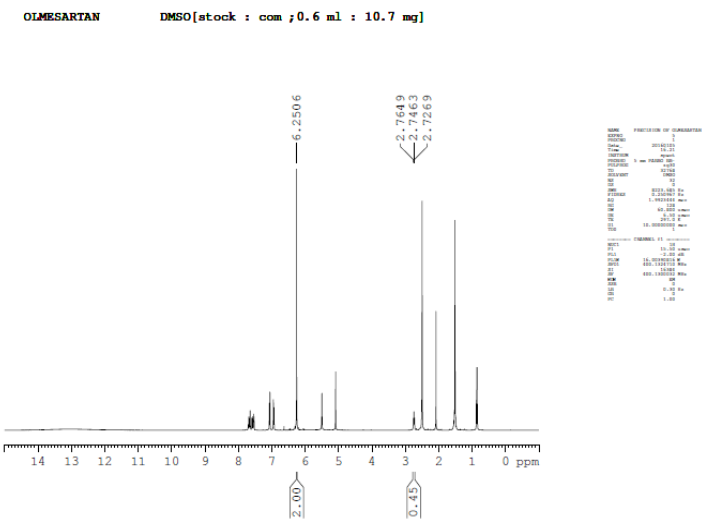


Fig.5.7.5 Intermediate Precision 10.7 mg + 0.6 ml stock

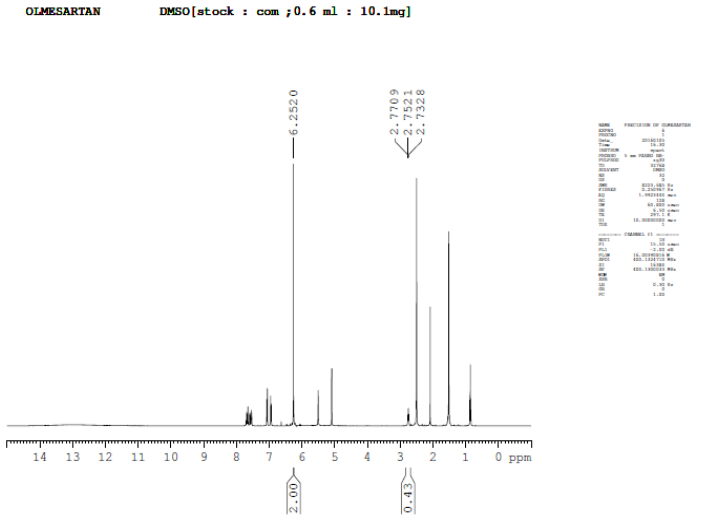


Fig.5.7.6 Intermediate Precision 10.1 mg + 0.6 ml stock

5.2.5 ACCURACY

The accuracy of an analytical method expresses the closeness of agreement between an accepted reference value and the value found. The accuracy of an analytical procedure should be established across its range. The ICH documents recommend that accuracy should be assessed using a minimum of nine determinations over a minimum of three concentration levels, covering the specified range.

Data from nine determinations over three concentration levels covering the specified range was determined. The accuracy was studied at 80,100 and 120% levels with respect to the sample by preparing the solutions in triplicate at each level. From the results as per Table, it

was concluded that method for assay content was accurate between the ranges of 80 to 120% level.% RSD at each level was level was found to be less than 2.00.

Objective: Quantitative analysis of given compound **OLMESARTAN by** NMR for accuracy.

Experiment: ^{1}H NMR, Solvent DMSO-d6.

Table:-5.4 ACCURACY

Accuracy Level		Taken Drug in mg	Found drug in mg	%Assay (as such)
80%	Set-1	8.10	8.10	100.00
80%	Set-2	8.25	8.34	101.06
80%	Set-3	8.32	8.34	100.22
100%	Set-1	10.00	10.00	100.06
100%	Set-2	10.35	10.48	101.28
100%	Set-3	10.41	10.48	100.69
120%	Set-1	12.25	12.39	101.13
120%	Set-2	12.14	12.15	100.08
120%	Set-3	12.40	12.63	101.83
			Mean	100.70
		Overall	SD	0.618
			%RSD	0.613

* I.S. is Maleic acid, M.W. = 116.06, Purity (A(B)= 99%

#COI is **OLMESARTAN**, M.W. =558.58.

Formula Used

$$Assay\ of\ the\ sample = \frac{I(A)\times MW(A)\times No.ofHs(B)\times W(B)\times A(B)}{No.ofHs(A)\times W(A)\times I(B)\times MW(B)}$$

Table:-5.4.1 Tabular representation of The accuracy parameter

Observations

No. of reading	Internal standard (B)*		Compound of interest (A)#		%age	Amount obtained
	Weight (mg)	Norm. Integration	Weight (mg)	Norm. Integration	Recovery	Weight (mg)
1st	10.00	2.00	8.10	0.34	100.00	8.10
2nd	10.00	2.00	8.25	0.35	101.06	8.34
3rd	10.00	2.00	8.32	0.35	100.22	8.34
4th	10.00	2.00	10.00	0.42	100.06	10.00
5th	10.00	2.00	10.35	0.44	101.28	10.48
6th	10.00	2.00	10.41	0.44	100.69	10.48
7th	10.00	2.00	12.25	0.52	101.13	12.39

8th	10.00	2.00	12.14	0.51	100.08	12.15
9th	10.00	2.00	12.40	0.53	101.83	12.63

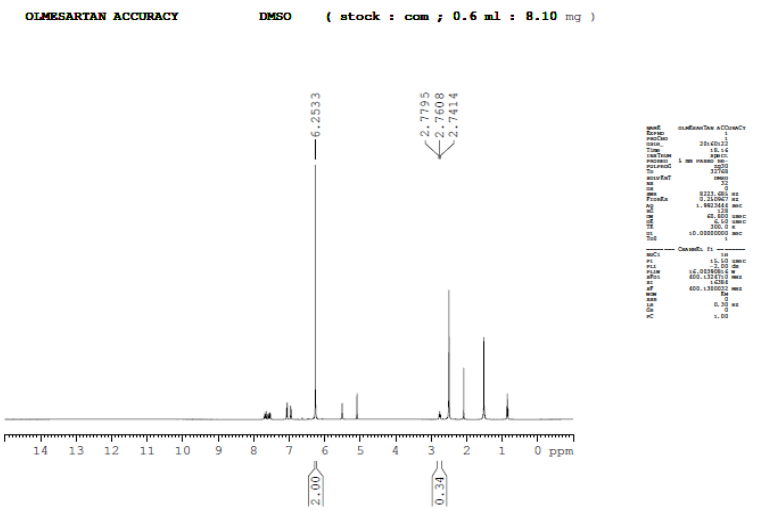


Fig.5.8.1 Accuracy 8.10 mg Std + 0.6 ml stock

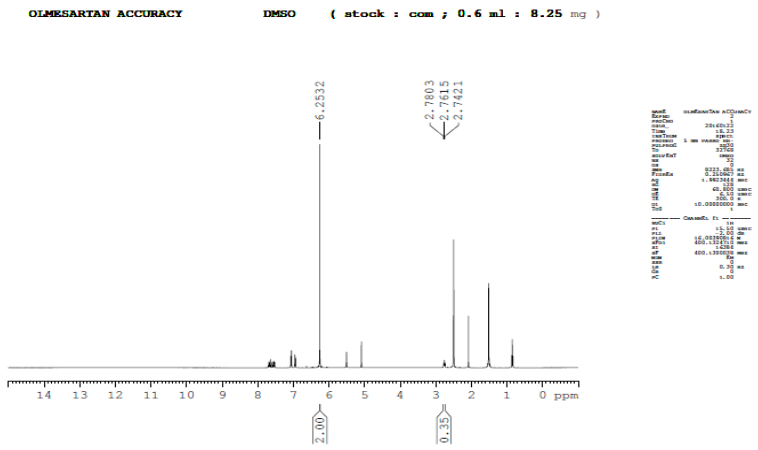


Fig.5.8.2 Accuracy 8.25 mg Std + 0.6 ml stock

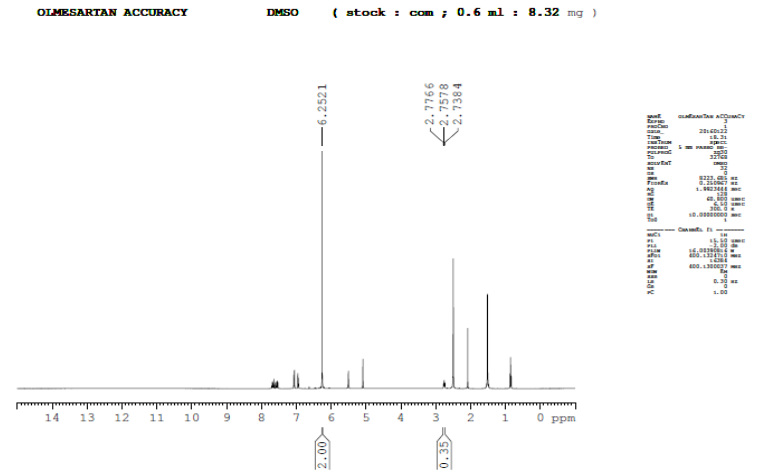


Fig.5.8.3 Accuracy 8.32 mg Std + 0.6 ml stock

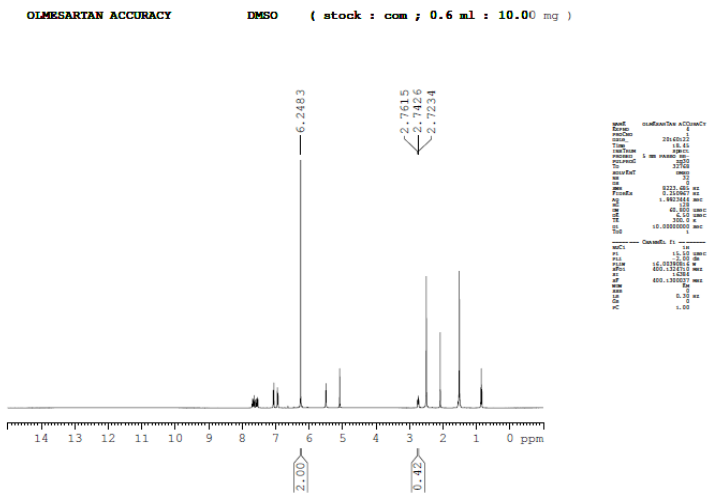


Fig.5.8.4 Accuracy 10.0 mg Std + 0.6 ml stock

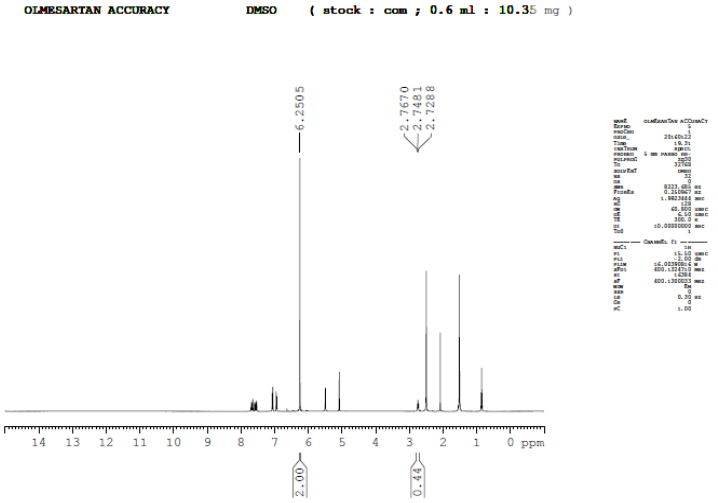


Fig.5.8.5 Accuracy 10.35 mg Std + 0.6 ml stock

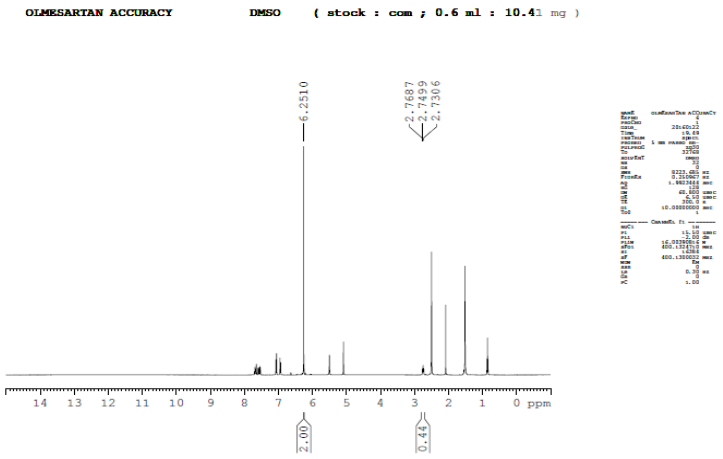


Fig.5.8.6 Accuracy 10.41mg Std + 0.6 ml stock

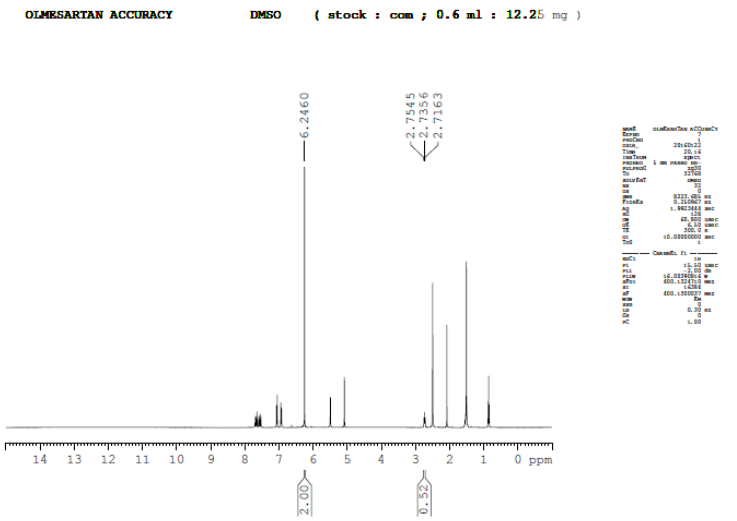


Fig.5.8.7 Accuracy 12.25 mg Std + 0.6 ml stock

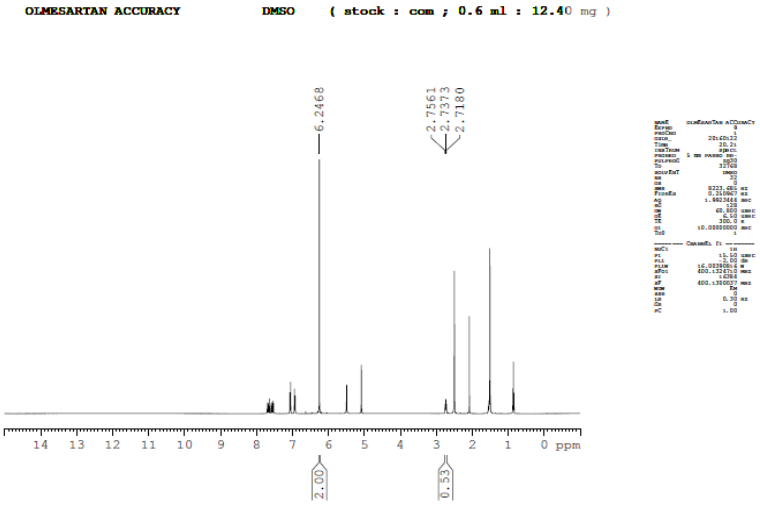


Fig.5.8.8 Accuracy 12.40 mg Std + 0.6 ml stock

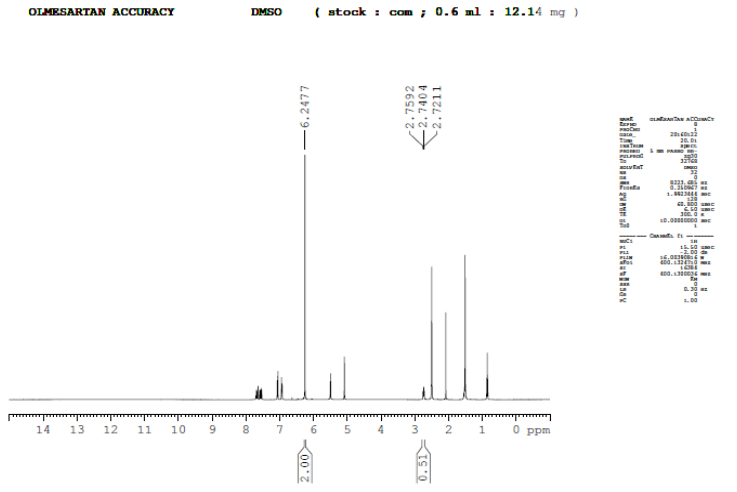


Fig.5.8.9 Accuracy 12.14 mg Std + 0.6 ml stock

5.2.6 ROBUSTNESS

The robustness of an analytical procedure is a measure of its capacity to remain unaffectedby small but deliberate variations in procedural parameters listed in the proceduredocumentation and provide an indication of its suitability during normal usage. Therobustness of the method was evaluated by varying two parameters independently: (1) Thenumber of scans (64 scans±16) and (2) The internal standard amount (20% variation) (10±2.0 mg). From the results obtained as per Table, running the experiment using a differentnumber of scans such as 48 or 80 rather than 64 did not affect the measurement. A variationof 20% in internal standard amount also did not appreciably change the measured amount of drug. Thereby, this method is quite robust in terms of the above-mentioned parameters.

Table:-5.5.1 Tabular representation of the Robustness parameter of Y-Drive

Parameter	Change	Found Drug in mg	%Assay (As such)	%Difference
Instrument	**JCL/ANAL/NMR/02**	**10.72**	**102.10**	**0.0**
Pulse Program	**Zg30**	**10.72**	**102.10**	**NA**
Time	**Fresh Sample**	**10.72**	**102.10**	**NA**
		Mean	**102.10**	
		SD	**1.74**	
		%RSD	**1.70**	

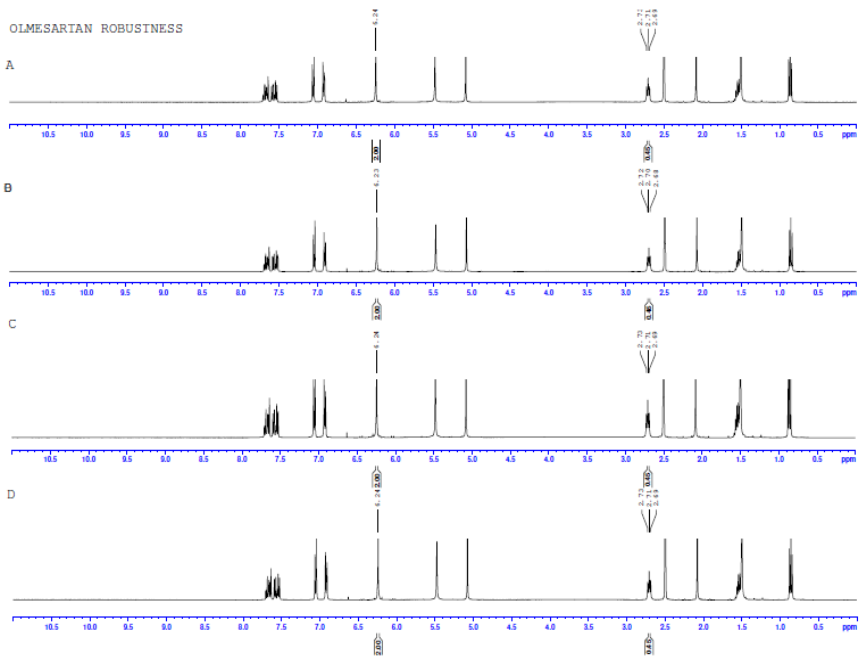


Fig.5.9.1 Robustness data on Bruker AV400 spectrometer in solvent Stock Solution

Table:- 5.5.2 Tabular representation of the Robustness parameter of Z-Drive

Parameter	Change	Found Drug in mg	%Assay (As such)	%Difference
Instrument	JCL/ANAL/NMR/03	4.97	211.00	0.0
Pulse Program	Zg	4.97	211.00	NA
Time	After 24 Hrs	4.97	211.00	NA
		Mean	211.00	
		SD	0.14	
		%RSD	0.06	

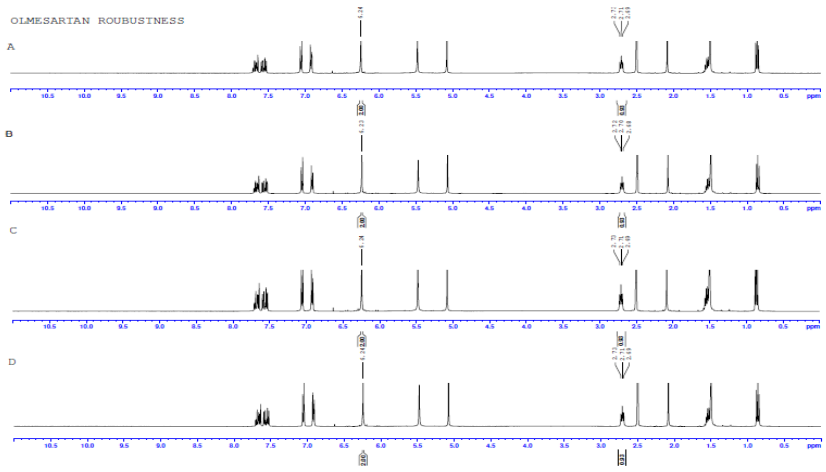


Fig.5.9.2 Robustness data on Bruker AV400 spectrometer in solvent Stock Solution

Table:- 5.6 Tabular representation of the Robustness parameter of Z-Drive

S.NO.	Change	Taken drug in mg	Found drug in mg	%Assay	%Difference
1	Fresh sample	10.20 mg	10.48	102.76	NA
2	After 24 Hours	10.20 mg	10.48	102.76	NA
3	After 48 Hours	10.20 mg	10.4	102.76	NA

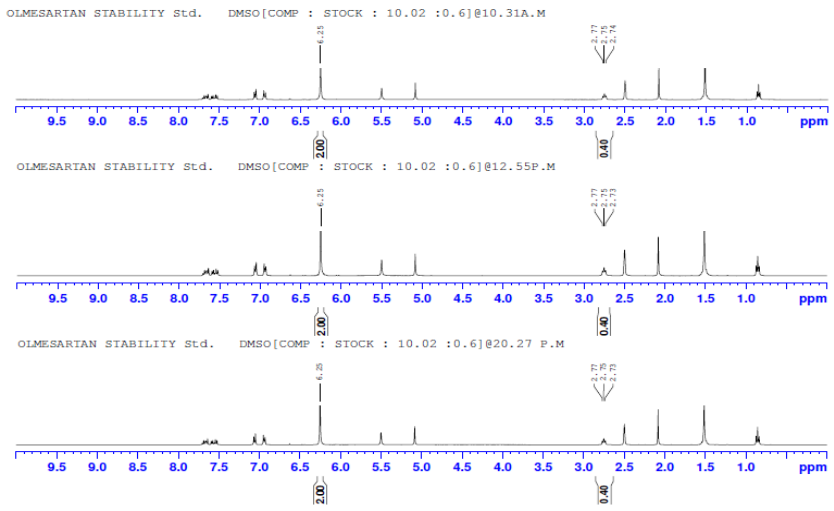


Figure:-5.10 Stability data on Bruker AV400 spectrometer in solvent Stock Solution

5.4 VALIDATION REPORT SUMMARY OF OLMESARTAN MEDOXOMIL

S.No.	Parameter	Experiment	Discussion	Acceptance criteria
1	**Specificity**	Interference to the IS and analyte proton	No interference at the 6.25 ppm and 2.75ppm.	No interference should be observed at IS peak and analyte proton.
2	**Linearity**	Coefficient of correlation (r)	0.999	≥ 0.99
3	**Precision**	Precision of six replicate samples prepared.	The R.S.D for six replicate preparations was found to be **0.3072**	The R.S.D for six replicate preparations should be not more than 2.0%
4	**Intermedi-ate Precision**	Analyst to analyst	The% RSD for % assay obtained from 6 precision samples was found to be **1.2922.**	The %RSD for % assay obtained from 6 precision samples should be not more than 2.0%.
5	**Accuracy**	Accuracy level 80%-120% and there triplicate	The % RSD for % assay obtained from 6 precision samples was found to be 0.6130.	The %RSD for % assay obtained from 6 precision samples should be not more than 2.0%.
6	**Robustness**	1]Changing thePulse Program (zg& zg30)	The % RSD for % assay obtained from robustness study was found **0.0612.**	The % RSD for % assay obtained from robustness study should be not more than 2.0%.
		2]changing the Instrument	The % RSD for % assay obtained from precision and robustness study was found **1.721.**	The % RSD for % assay obtained from robustness study should be not more than 2.0%.

CONCLUSION

The Assay method validation performed on drug substance **Olmesartan Medoxomil** gives specific, precise, linear and accurate results for the method. The Assay method for **Olmesartan Medoxomil** is also reproducible. **Hence the assay method for Olmesartan Medoxomilcan be used for routine analysis.**

ACKNOWLEDGEMENTS

It is great pleasure for me to acknowledge all those who have contributed towards the conception, origin and nurturing of this project.

With a deep sense of gratitude and the respect, I thank my esteemed research guide **Mr. Rajnish Kumar, Assistant Professor**, Department of Pharmaceutical Chemistry, Noida Institute of Technology, Greater Noida for his inestimable guidance, valuable suggestions and constant encouragement during the course of this study.

I am thankful to **Dr A. Mazumder**, Director, & **Dr. R. Mazumder**, Dean (R& D) for their constant moral, selfless support and directions Throughout the investigation. & I am thankful to **Mr. Kartikeya Dwivedi, Senior Research Associate-II & Sachin Kumar Bhullar Senior Research Associate-II, Manish Mitra, Abhishek kumar Research Associate Jubilant Chemsys Limited Noida, U.P** for their constant moral support, valuable suggestions, directions and selfless support throughout the investigation.

I am also grateful to **Dr. Partha Mukharjee, Senior Research Scientist Jubilant Chemsys Limited Noida, U.P** for their guidance during the project work.

At this moment, I thanks with deep gratitude to **my classmates** and **friends** for their moral support, constant encouragement and patience absolutely needed to complete my entire study. It was the blessing of them that gave me courage to face the challenges and made my path easier.

I am indebted infinitely to care, support and trust being shown by my parents without whom it would not be possible to complete this project.

Jeetendra Kumar **2014-2016**

REFERENCES

1. Gadape, H. and K. Parikh, Quantitative determination and validation of Olmesartan in pharmaceutical using quantitative nuclear magnetic resonance spectroscopy, J. Chemestry Pharma Resurch, 2011; 649-664.
2. Gallo. Vito, Nicola intini and Rober to consonni, Performance assessment in fingerprinting and multi component quantitative NMR analyses. Analytical Chemistry, 2015; 29-120.
3. Yang.Q, HQiu, WGuo, D.wang.Quantitative $_1$H-NMR Method for the Determination of Tadalafil in Bulk Drugs and its Tablets. Molecules, 2015; 145-334.
4. Yang.Q, HQiu, WGuo, D.wang. Quantitative $_1$H-NMR Method for the Determination of Tadalafil in Bulk Drugs and its Tablets. Molecules, 2015; 145-334.
5. Zhang, Yingru, HQiu, WGuo, D Wang, Enantiomer selective chromatography in drug discovery. Drug discovery today, 2015; 10(8): 145-334.

6. Shahina, S, Amit S. Minase, Manjusha N. Dole, Sanjay D. Sawant Analytical Method Development and Olmesartan medoxomil in Combined Tablet Dosage Form. Int. J. Med. 2011; 20-103.
7. Wu, Y, National Institutes for Food and Drug Control, Tiantan Xili 2, Beijing 100050, China. Application of quantitative 1H NMR for the calibration of protoberberine alkaloid reference standards. Journal of pharmaceutical and biomedical analysis, 2013; 90-92.
8. Holzgrabe, U, B.W. Diehl, and I. Wawer, NMR spectroscopy in pharmacy. Journal of pharmaceutical and biomedical analysis, 1998; 17(4): 557-616.
9. Kumar, A, NMR a preeminent technique in pharmaceutical analysis. Acta Poly Pharm, 2012; 69(3): 371-380.
10. O, Neil M J, The Merk Index- an encyclopedia of chemicals and biological drugs 15th Edithons, Cambridge, UK15BN9781849736701, 2013, P.2708.
11. Holzgrabe, U, B.W. Diehl and I. Wawer, NMR spectroscopy in pharmacy. Journal of pharmaceutical and biomedical analysis, 1998; 17(4): 557-616.
12. V.Rizzo; V Pinciroli. Journal of Pharmaceutical and Biomedical Analysis, 2005; 38: 851-857.
13. Okeke and Abbas, S.S. Wang, XRLIG Stability-Indicating Determination of Olmesartan medoxomil in the Presence of its Acid Degradation Products. Journal of AOAC International, 2014; 97(1): 78-85.
14. Yang.Q, HQiu, WGuo, D.wang. Quantitative $_1$H-NMR Method for the Determination of Tadalafil in Bulk Drugs and its Tablets. Molecules, 2015; 145-334.
15. Guideline, I. Q2 (R1) (2005) Validation of analytical procedures: text and methodology. in International conference on harmonization. 1996; 204-220.
16. Moustafa, A.A. and L.I. Bibawy, Stability-indicating assay of Olmesartan in the presence of its degradation products. Spectroscopy letters, 1999; 1073-1098.
17. Chaudhari.P, P.Bhalerao Method validation for spectrophotometric estimation of Cilnidipine in combined tablet dosage form. Int J Pharm Pharm Sci. 2012; 4(5): 96-98.