Method Development, Validation and Stability Study by UV Spectroscopic and HPLC Method For Olanzapine in Bulk and Pharmaceutical Dosage Forms

Meenu Chaudhary*, Praveen Kumar[1], Anjali Gusain[2]
School of Pharmaceutical Sciences,
Shri Guru Ram Rai University, Dehradun, India

Abstract: A simple, unique and dependable UV-VIS spectrophotometric method used to be as soon as developed for the estimation of Olanzapine in bulk and pharmaceutical dosage forms. Water: Hydrochloric acid (9:1) was chosen as the solvent system. The λmax was discovered to be 257 nm and the response Lenier in the vary of 2-12µg/ml. The regression equation of the calibration format and correlation coefficient had been found to be Y = 0.0779+0.002 and 1.0 respectively. The %RSD values for each intraday and interday precision had been less than 1% the recovery of the drug from the pattern was once in precise ranged.

The proposed approach used to be validated for accuracy, precision, robustness, ruggedness, LOD and LOQ whilst estimating the commercial components there was no interference of excipients and other additives. Stability study of olanzapine (Dosage Form) was carried out Accelerated study, which was perform at 40°C ± 2°C Temperature and 75% ± 5% RH (Relative Humidity) for 1st, 3rd and 6th Months. Similarly Long Term Stability study of Olanzapine (Dosage Forms) was carried out at 30°C ± 2°C Temperature and 75% ± 5% RH (Relative Humidity) for 3st, 6rd and 9th Months.

***Key Word*: Olanzapine, UV-VIS Spectrophotometric, Validation Study and Stability Study.**

1. INTRODUCTION

Drug stability refers to the capacity of the drug substance or product to remain within established specification of identification, strength, quality and purity in a specified period of time. Stability is officially defined as the time laps during which the drug product retains the same properties characteristics that is proposed at the time of manufacture. The stability of the product is expressed as the expiry period or technically as shelf life. [1,2]

Objective of the Stability Study:

The guidelines for stability study are given by ICH: [3,4]

Q1A (R2): Stability testing of new drug substance and products

Q1B: Stability testing: photo stability testing of new drug substance and products

Q1C: Stability testing of new dosage forms

Q1D: Bracketing and matrixing design for stability testing of new drug substances and products

Q1E: Evaluation of stability studies.

Q1F: Stability Data Package for Registration Applications in Climatic Zones III and IV

TYPES OF STABILITY TESTING:

Stability testing is a typical technique performed on calm substances and items and is used at various periods of the item change. In starting occasions, stimulated dependability testing (at reasonably high temperatures and also clamminess) is used as a piece of demand to choose the kind of debasement items which may be found after whole deal accumulating. Testing under less intensive conditions i.e. those endorsed for whole deal rack amassing, at possibly lifted temperatures is used to choose an item's time allotment of sensible ease of use and slip by dates. [5, 6]

1) Long Term Stability Testing:

Long Term stability testing is routinely performed for longer term of the preliminary with a particular ultimate objective to allow important item degradation under proposed accumulating conditions. The season of the test depends on the quality of the item which should be adequately long to show clearly that no quantifiable degradation occurs and ought to enable one to perceive debasement from between measure assortment. In the midst of the testing, data is accumulated at an appropriate repeat with the true objective that an example examination can perceive precariousness think about from ordinary unclearness. The constancy of data interpretation can be extended by including a singular bunch of reference material for which security characteristics have quite recently been developed. [7, 8]

2) Accelerated Stability Testing:

In accelerated stability testing, an item is stressed at a couple of high (more sizzling than including) temperatures and the proportion of warmth input required to cause item dissatisfaction is settled. This is done to subject the item to a condition that revives corruption. This information is then foreseen to anticipate time span of practical ease of use or used to investigate the relative soundness testing of elective definitions. This for the most part gives an early indication of the item time range of ease of use and thusly shortening the refrigerated consequent to pushing, and after that tried in the meantime. Since the length of the examination is short, the likelihood of instability in the estimation structure is lessened in relationship progression plan. Quickened strength testing relies upon the Arrhenius condition (1) and balanced Arrhenius condition. [9, 10, 11]

$$K = Ae^{-E_a/(RT)}$$

$$\ln(K) = \frac{-Ea}{RT} + \ln(A)$$

Where,

K = degradation rate

A = Frequency factor/s

ΔE = Activation energy **(kJ/mol)**

R = Universal gas constant (**0.00831kJ/mol**)

T = Absolute temperature **(K)**

As modified. Equation:

$$K = A\,(T/T_0)^n .\, e^{-Ea/(RT)}$$

These conditions depict the connection between capacity temperatures and corruption rate. Utilizing Arrhenius condition, projection of solidness from the debasement rates saw at high temperatures for some corruption procedures can be resolved. At the point when the actuation vitality is known, the corruption rate at low temperatures might be anticipated from those seen at **"STRESS"** temperatures.

Table 1.1: ICH Stability Zones.

ZONE	TYPES OF CLIMATE
Zone **1**	Mediterranean / Subtropical zone
Zone **2**	Hot dry zone
Zone **3**	Hot humid/Tropical zone
Zone **4 a**	ASEAN testing conditions
Zone **4 b**	Hot / Higher humidity

Table 1.2: Long Term Testing Conditions.

Climate Zone	Temperature	Humidity	Minimum Duration
Zone **1**	21°c ± 2°c	45 % ± 5 % RH	12 Months
Zone **2**	25°c ± 2°c	60 % ± 5 % RH	12 Months
Zone **3**	30°c ± 2°c	35 % ± 5 % RH	12 Months
Zone **4 a**	30°c ± 2°c	65 % ± 5 % RH	12 Months
Zone **4 b**	30°c ± 2°c	75 % ± 5 % RH	12 Months
Refrigerated	5°c ± 3°c	No Humidity	12 Months
Frozen	-15°c ± 5°c	No Humidity	12 Months

Table 1.3: Accelerated and Intermediate Testing Conditions:

Test Type	Temperature	Humidity	Minimum Duration
Accelerated Ambient	40 °c ± 2°c	75 % ± 5 % RH	6 Months
Accelerated Refrigerated	25 °c ± 2°c	60 % ± 5 % RH	6 Months
Accelerated Frozen	5 °c ± 3°c	No Humidity	6 Months
Intermediate	30 °c ± 2°c	65 % ± 5 % RH	6 Months

MATERIALS AND METHODS

Materials which are used for study of validation and Stability study of olanzapine and its dosage forms are given as well as following.

Table 1.4: - **List of Chemicals used for Analytical Study of Olanzapine**

S.No.	Drug / Excipient / Solvent	Manufacturer / Supplier
1.	Olanzapine (API)	Gift Sample
2.	Hydrochloric Acid	Rankem A Grade
3.	Methanol	Rankem A Grade
4.	Acetonitrile (ACN)	Rankem A Grade

Table No- 1.5. List of Equipment's used for Analytical Study of Olanzapine

S. No.	Instruments / Glassware's	Manufacturer/ Supplier
1.	UV-visible double Beam Spectrophotometer	Schimadzu, Mumbai
2.	High Pressure Liquid Chromatography (HPLC)	Agilent
3.	Mechanical stirrer	Remi Elektrotech Ltd, Mumbai
4.	Analytical Weighing Balance	Citizone
5.	Digital Sonicator	Rivotek
6.	Digital pH meter	Systronics, Delhi
7.	Digital melting point apparatus	Perfit, Ambala cant
8.	Magnetic stirrer	Remi Elektrotech Ltd, Mumbai

9.	Volumetric Glass	Borosil A Grade
10.	Measuring Cylinder	Borosil A Grade
11.	Graduate Pippete	Borosil A Grade
12.	Bulb Pippete	Borosil A Grade
13.	Glass Beaker	Borosil A Grade

METHODS:

1. IDENTIFICATION OF DRUG:-

A. Organoleptic Characteristics:-

The color, Odor, and taste of the drug were characterized and recorded.

B. Determination of Melting point:

The drug will be filled in one end fused Capillary tube and kept into digital melting point apparatus. The apparatus will operated and the temperature at which drug will start melting will be noted as melting point**.**

C. Determination The wavelength (λ_{max}) of Olanzapine in 0.1 N HCl:-Standard stock solution of Olanzapine prepared by dissolving 50 mg of Olanzapine in 50 ml of 0.1 N HCl and sonicated for 15 minutes in bath Sonicator and prepares dilution of 1 mg/1 ml i.e. 1000 µg/ml (1000 ppm) stock solution. From this stock solution prepared 10 µg/ml solutions. Scan the sample at their standard λ_{max} and determine the wavelength of Olanzapine

D. Preparation of standard plot of Olanzapine in 0.1 N HCl: -

Standard stock solution of Olanzapine will be prepared by dissolving 50 mg of Olanzapine in 50 ml of 0.1 N HCl and sonicated for 15 minutes in bath Sonicator and prepare dilution of 1 mg/1 ml i.e. 1000 µg/ml (1000 ppm) stock solution. From this stock solution we can prepare 2-12 ppm solution, scan the sample at their standard λ_{max} and prepared standard plot of olanzapine.

VALIDATION PARAMETER:

1. **Accuracy:** The accuracy of an analytical procedure expresses the closeness of agreement between the value which is accepted either as a conventional true value or an accepted reference value and the value found. This is sometimes termed trueness. The accuracy data are given in table.[12]
2. **Precision:** The precision of an analytical procedure expresses the closeness of agreement (degree of scatter) between a series of measurements obtained from multiple sampling of the same homogeneous sample under the prescribed conditions. Precision may be considered at three levels: repeatability, intermediate precision and reproducibility. Precision should be investigated using homogeneous, authentic samples. However, if it is not possible to obtain a homogeneous sample it may be investigated using artificially prepared samples or a sample solution. The precision of an analytical procedure is usually expressed as the variance, standard deviation or coefficient of variation of a series of measurements. The precision data are given in ta. Precision is further subdivided into two parts: [13]

a. **Intra-day Precision:**

Intra-day precision simply means within run which assesses precision during a single analytical run.

b. **Inter-day precision**

Inter-day precision simply means between-run which measures precision with time, and may involve different analysts, equipment, reagents, and laboratories.

3. Robustness/ Ruggedness

The definition for robustness/ruggedness applied is the robustness/ruggedness of an analytical procedure is a measure of its capacity to remain unaffected by small, but deliberate variations in method parameters and provides an indication of its reliability during normal usage. Robustness can be described as the ability to reproduce the (analytical) method in different laboratories or under different circumstances without the occurrence of unexpected differences in the obtained results, and a robustness test as an experimental set-up to evaluate the robustness of a method. The term ruggedness is frequently used as a synonym. Several definitions for robustness or ruggedness exist which are, however, all closely related.

4. Limit of Detection

LOD: The Limit of Detection (LOD) of an individual analytical procedure is the lowest amount of analyte in a sample, which can be detected but not necessarily quantitated as an exact value

determined with statistical method by using Statistical formula. The limit of Detection (L.O.D.) was calculated as per below equation:

$$\textbf{Limit of Detection} = \frac{3.3 * \textbf{S.D.}}{\textbf{Slope}}$$

5. Limit of Quantitation

The Limit of quantification (LOQ) of an individual analytical procedure is the lowest amount of analyte in a sample, which can be quantitatively determined with statistical method by using statistical formula. The limit of Quantification (LOQ) was calculated as per below equation:

$$\textbf{Limit of Quantitation} = \frac{10.0 * \textbf{S.D.}}{\textbf{Slope}}$$

RESULT AND DISCUSSION:

1. IDENTIFICATION STUDY:-

A. Organoleptic Characteristics:-

Table No. – 1.6: The Organoleptic Properties of Olanzapine as well as following,

S.NO.	Organoleptic Properties	Result
1.	Color	Yellow crystalline Powder
2.	Odor	Characteristics
3.	Taste	Characteristics

B. Determination of Melting Point

Melting point of Olanzapine was found to be 195.21 ± 0.95°C (Table 1.5). From the observation of the melting point, the drug can be considered to be sufficiently pure for employing it is present investigation. Melting point in Merck Index is 190-195°C.

Table No. 1.7: - Result of Melting Point Determination of Olanzapine.

Observed Melting Point (°C)	Mean ± S.D. (n =3)

Sample 1	Sample 2	Sample 3	
194.66	195.40	195.58	195.21 ± 0.95

2. RESULT OF ANALYSIS:

A. Standard Curve of Olanzapine in 0.1 N HCl:-

The standard plots of Olanzapine were prepared in 0.1 N HCl. This indicate that the standard curve of Olanzapine in above media followed Beer law, R^2 values were found to be in between 1.0, the linear regression equation can be used of Olanzapine is 0.1 N HCl media.

Final Wavelength (λ_{max}) of Olanzapine is = 257 nm in 0.1N HCl Media

Table No 1.8:- Standard Plot of Olanzapine in 0.1 N HCl.

S. No.	Concentration (µg/ml.)	Absorbance			Mean ± S.D.
		Sample 1	Sample 2	Sample 3	
1.	**Blank**	0.0000	0.0000	0.0000	0.0000 ± 0.0000
2.	2.0	0.155	0.160	0.159	0.158 ± 0.002
3.	4.0	0.315	0.311	0.316	0.314 ± 0.002
4.	6.0	0.486	0.476	0.469	0.471 ± 0.004
5.	8.0	0.620	0.628	0.630	0.626 ± 0.005
6.	10.0	0.778	0.784	0.781	0.781 ± 0.003
7.	12.0	0.930	0.935	0.934	0.934 ± 0.003

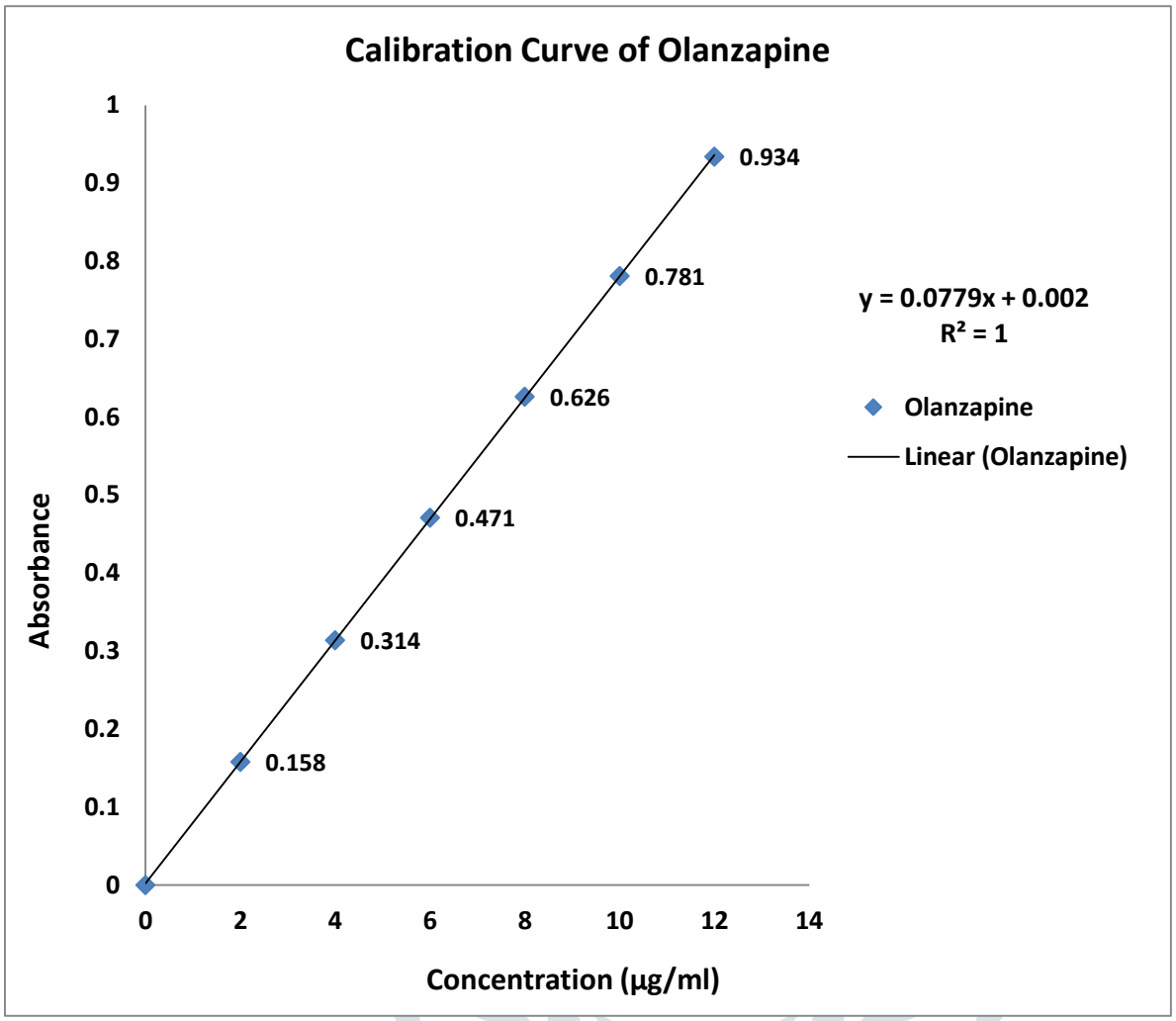

Figure 1: - Calibration Curve of Olanzapine.

Table No. 1.9:- Regression equation and correlation coefficient of Olanzapine in 0.1 N HCl.

S. No	Media	Regression Equation	Correlation Coefficient (R^2)
1.	0.1 N HCl	Y= 0.0779x + 0.002	1.0

VALIDATION RESULTS OF OLANZAPINE:

1. ACCURACY:

Table 2.0: Accuracy Data of the UV-VIS Spectrophotometric Method for Olanzapine

Sample	Concentration (µg/ml.)		Absorbance	% Recovery	Statistical Analysis
	Pure Concentration	Final Concentration			
S_1:80%	8	10	0.611	97.72	**Mean:-98.52 S.D.- 0.73 % RSD- 0.74**
S_2:80%	8	10	0.620	99.16	
S_3:80%	8	10	0.617	98.68	
S_4:100%	10	10	0.780	99.87	**Mean:-99.22 S.D.- 1.45 % RSD- 1.46**
S_5:100%	10	10	0.762	99.56	
S_6:100%	10	10	0.783	100.25	
S_7:120%	12	10	0.928	99.05	**Mean:-99.44 S.D.- 0.50 % RSD- 0.51**
S_8:120%	12	10	0.937	100.02	
S_9:120%	12	10	0.930	99.27	

2. PRECISION:

(a.) Repeatability:

Table 2.1: Precision Data Showing Repeatability of the UV-VIS Spectrophotometric Method for Olanzapine.

S.No.	Concentration (µg/ml.)	Absorbance	Calculated Amount (µg/ml.)	Statistical Analysis
1.	10	0.788	10.08	**Mean:- 10.06 S.D.- 0.067 % RSD- 0.67**
2.	10	0.780	9.98	
3.	10	0.786	10.06	
4.	10	0.781	10.0	
5.	10	0.790	10.11	
6.	10	0.794	10.16	

(b.) Intraday Precision:

Table 2.2: Intra Day Precision Data of the UV-VIS Spectrophotometric Method for Olanzapine

Concentration (µg/ml.)	Absorbance-1	Absorbance-2	Absorbance-3	Statistical Analysis

10	0.782	0.783	0.782	
10	0.790	0.779	0.785	
10	0.780	0.782	0.779	
10	0.776	0.786	0.787	**Mean:- 10.02**
10	0.788	0.790	0.785	**S.D.- 0.01**
10	0.784	0.781	0.791	**% RSD- 0.09**
MEAN	**0.783**	**0.782**	**0.784**	
Cal. Amount (µg/ml.)	**10.02**	**10.01**	**10.03**	

(c.) Interday Precision:

Table 2.3: Inter Day Precision Data of the UV-VIS Spectrophotometric Method for Olanzapine

Concentration (µg/ml.)	Absorbance (Day-1)	Absorbance (Day-2)	Absorbance (Day-3)	Statistical Analysis
10	0.783	0.787	0.774	
10	0.787	0.780	0.785	
10	0.792	0.790	0.778	
10	0.790	0.783	0.784	**Mean:- 10.0**
10	0.781	0.780	0.775	**S.D.- 0.020**
10	0.776	0.776	0.789	**% RSD- 0.20**
MEAN	**0.784**	**0.782**	**0.780**	
Cal. Amount (µg/ml.)	**10.03**	**10.01**	**9.98**	

3. Ruggedness Data:

Table 2.4: Ruggedness Data of the UV-VIS Spectrophotometric Method by Different Analyst for Olanzapine.

ANALYST-1				ANALYST-2			
Conc^n	**Abs.**	**Cal. Amt.**	**Statistical**	**Conc^n**	**Abs.**	**Cal.**	**Statistical**

(µg/ml.)		(µg/ml.)	Analysis	(µg/ml.)		Amt. (µg/ml.)	Analysis
10	0.792	10.14		10	0.786	10.06	
10	0.785	10.05		10	0.778	9.96	
10	0.789	10.10		10	0.784	10.03	
10	0.784	10.03	Mean:- 10.5 S.D.- 0.061 % RSD- 0.61	10	0.790	10.11	Mean:- 10.0 S.D.- 0.020 % RSD- 0.20
10	0.779	9.97		10	0.787	10.07	
10	0.782	10.01		10	0.783	10.02	

4. Robustness Data:

Table 2.5: Robustness Data of the UV-VIS Spectrophotometric Method by Different Analyst for Olanzapine.

WATER: HCl (90:10)				WATER: HCl (85:15)			
Conc^n (µg/ml.)	Abs.	Cal. Amt. (µg/ml.)	Statistical Analysis	Conc^n (µg/ml.)	Abs.	Cal. Amt. (µg/ml.)	Statistical Analysis
10	0.774	9.91		10	0.783	10.02	
10	0.786	10.06		10	0.775	9.92	
10	0.776	9.93		10	0.788	10.08	
10	0.790	10.11	Mean:- 10.01 S.D.- 0.08 % RSD- 0.80	10	0.781	10.0	Mean:- 10.01 S.D.- 0.072 % RSD- 0.72
10	0.787	10.07		10	0.777	9.94	
10	0.784	10.03		10	0.789	10.10	

5. Limit of Detection (LOD) & Limit of Quantitation (LOQ): -

Table 2.6: Limit of detection and Limit of quantitation of Olanzapine by UV-VIS Spectrophotometric Method.

S.No.	Parameter	Standard Deviation	Slope	Formula	Calculation (µg/ml.)

1.	**Limit od Detection (LOD)**	0.009	0.0779	3.3*(S.D./Slope)	0.381
2.	**Limit of Quantitation (LOQ)**	0.009	0.0779	10*(S.D./Slope)	1.15

STABILITY STUDY OF OZACE MD-10 TABLET (OLANZAPINE USP):

The stability study of olanzapine (Dosage Forms) was carried out on the Accelerated and Long Term stability study with marketed formulations.

Table 2.7: Marketed formulation of Olanzapine USP given as bellow.

S. No.	GENERIC NAME	MARKET FORMULATION	BATCH NO.
1.	Olanzapine USP	Ozace MD-10 mg	**CAF28001**
2.	Olanzapine USP	Ozace MD-10 mg	**CAF28002**
3.	Olanzapine USP	Ozace MD-10 mg	**CAF28003**

Chromatographic Condition:

Buffer: Dissolve 3.0 gram of Ammonium Dihydrogen Phosphate in 1000 ml of water add 2 ml of Trimethylamine and adjust the PH – 2.5 with Orth phosphoric acid, mix and filter through 0.45µ filter paper.

Mobile Phase: 60 Volume of Buffer: 20 Volume of ACN: 20 Volume of Methanol.

Column: C 18, (250×4.6 mm, 5µm), Make-Cosmosil, 5C18-MS-II or Equivalent.

Column Temperature: 30°C

Flow Rate: 1.0 ml/Minute

Detector: 220 nm

Injection Volume: 20 µL.

Diluent: Mobile Phase.

Accelerated and Long Term Stability Study of Ozace MD-10 mg Tablet:

1. Accelerated Stability Study of Ozace MD-10 mg Tablet (Specification of Initial Data):

The Specification of initial stability data of Ozace MD-10 mg tablet is given as following finish good products in below table.

Table 2.8: Accelerated Stability Study of Ozace MD-10 mg tablet are given as bellow of Initial Condition.

S.NO.	TESTS	OBSERVATION	SPECIFICATION
1.	**Description**	Yellow coloured, elongated, biconvex, scored on one side and plain on other side, Uncoated Mouth Dissolving tablet.	Yellow coloured, elongated, biconvex, scored on one side and plain on other side, Uncoated Mouth Dissolving tablet.
2.	**Identification by HPLC**	Complies	In the Assay, the principal peak in the chromatogram obtained with the test solution corresponds to the peak in the chromatogram obtained with standard solution.
3.	**Average Weight**	169.0 mg	170.0 mg ± 4.0 %
4.	**Uniform of content Olanzapine USP**	99.5% to 103.8 %	85% to 115% of average content
5.	**Disintegration Time**	22 Second	NMT 3.0 Minute
6.	**Assay (By HPLC)**	100.9 %	97% to 110% of Label Claim
7.	**Friability**	0.23 %	NMT 1%
8.	**Hardness**	3.98 to 4.86 kg/cm^2	NLT 2 kg/cm^2

2. Accelerated Stability Study of Ozace MD-10 mg Tablet (1st-MONTH), 40°C/75%RH:

The 1st Month accelerated stability data of Ozace MD-10 mg tablet is given as following below table.

Table 2.9: Accelerated Stability Study of Ozace MD-10 mg tablet are given as bellow of 1st Month.

S.NO.	PARAMETER	ANALYTICAL STASTICAL DATA

1.	**Description**	Yellow coloured, elongated, biconvex, scored on one side and plain on other side, Uncoated Mouth Dissolving tablet.
2.	**Average Weight**	170.10 mg ± 4.0 %
3.	**Disintegration Time**	22 Second
4.	**Hardness**	3.5 kg/cm^2
5.	**Friability**	0.22 %

6.	**Assay (By HPLC)**				**%ASSAY** ↓		
	Area of Standard	**Area of Sample**					
		BATCH NO.					
		CAF28001	**CAF28002**	**CAF28003**			
	8563791	8616449	8839319	8837378	**10**	**102.7**	**102.9**
	8577547						
	8597386						
	8602533	8617860	8745888	8768249			
	8580651				**0.1**		
MEAN	**8584382**	**8617155**	**8792604**	**8802814**			
Standard Deviation	15677.93						
% RSD	0.18						

3. Accelerated Stability Study of Ozace MD-10 mg Tablet (3rd-MONTH), 40°C/75%RH:

The 3rd Month accelerated stability data of Ozace MD-10 mg tablet is given as following below table.

Table 2.10: Accelerated Stability Study of Ozace MD-10 mg tablet are given as bellow of 3rd Month.

S.NO.	PARAMETER	ANALYTICAL STASTICAL DATA
1.	**Description**	Yellow coloured, elongated, biconvex,

<table>
<tr><td></td><td colspan="4"></td><td colspan="3">scored on one side and plain on other side, Uncoated Mouth Dissolving tablet.</td></tr>
<tr><td>2.</td><td colspan="4">Average Weight</td><td colspan="3">169.75 mg ± 4.0 %</td></tr>
<tr><td>3.</td><td colspan="4">Disintegration Time</td><td colspan="3">25 Second</td></tr>
<tr><td>4.</td><td colspan="4">Hardness</td><td colspan="3">3.7 kg/cm^2</td></tr>
<tr><td>5.</td><td colspan="4">Friability</td><td colspan="3">0.21 %</td></tr>
<tr><td rowspan="10">6.</td><td colspan="4">Assay
(By HPLC)</td><td colspan="3" rowspan="3">%ASSAY
↓</td></tr>
<tr><td rowspan="2">Area of Standard</td><td colspan="3">Area of Sample</td></tr>
<tr><td colspan="3">BATCH NO.</td></tr>
<tr><td>CAF28001</td><td>CAF28002</td><td>CAF28003</td><td rowspan="6">101.1</td><td rowspan="6">100.8</td><td rowspan="6">102.4</td></tr>
<tr><td>98958105</td><td rowspan="3">98171722</td><td rowspan="3">98472901</td><td rowspan="3">96755638</td></tr>
<tr><td>97264976</td></tr>
<tr><td>97075418</td></tr>
<tr><td>98448557</td><td rowspan="2">98032021</td><td rowspan="2">98066073</td><td rowspan="2">97662839</td></tr>
<tr><td>97851477</td></tr>
<tr><td>MEAN</td><td>97919707</td><td>98101872</td><td>98269487</td><td>97209239</td></tr>
<tr><td>Standard Deviation</td><td colspan="4">791218.15</td></tr>
<tr><td>% RSD</td><td colspan="4">0.80</td></tr>
</table>

4. Long Term Stability Study of Ozace MD-10 mg Tablet (3rd- MONTH), 30°C/75%RH:

The 3rd Month Long Term stability data of Ozace MD-10 mg tablet is given as following below table.

Table 2.11: Long Term Stability Study of Ozace MD-10 mg tablet are given as bellow of 3rd Month.

S.NO.	PARAMETER	ANALYTICAL STASTICAL DATA
1.	**Description**	Yellow coloured, elongated, biconvex, scored on one side and

					plain on other side, Uncoated Mouth Dissolving tablet.		
2.	**Average Weight**				169.75 mg ± 4.0 %		
3.	**Disintegration Time**				25 Second		
4.	**Hardness**				3.7 kg/cm^2		
5.	**Friability**				0.21 %		
6.	**Assay (By HPLC)**				**%ASSAY** ↓		
	Area of Standard	**Area of Sample**					
		BATCH NO.					
		CAF28001	**CAF28002**	**CAF28003**			
	98958105	98553652	98140941	98249961	**101.5**	**102.7**	**101.3**
	97264976						
	97075418						
	98448557	98234877	98030702	98323000			
	97851477						
MEAN	**97919707**	**98394265**	**98085822**	**98286481**			
Standard Deviation	791218.15						
% RSD	0.80						

5. Accelerated Stability Study of Ozace MD-10 mg Tablet (6th-MONTH), 40°C/75%RH:

The 6th Month accelerated stability data of Ozace MD-10 mg tablet is given as following below table.

Table 2.12: Accelerated Stability Study of Ozace MD-10 mg tablet are given as bellow of 6th Month.

S.NO.	PARAMETER	ANALYTICAL STASTICAL DATA
1.	**Description**	Yellow coloured, elongated, biconvex, scored on one side and plain on other side,

<table>
<tr><td></td><td colspan="5"></td><td>Uncoated Mouth Dissolving tablet.</td></tr>
<tr><td>2.</td><td colspan="5">Average Weight</td><td>169.08 mg ± 4.0 %</td></tr>
<tr><td>3.</td><td colspan="5">Disintegration Time</td><td>28 Second</td></tr>
<tr><td>4.</td><td colspan="5">Hardness</td><td>3.8 kg/cm^2</td></tr>
<tr><td>5.</td><td colspan="5">Friability</td><td>0.24 %</td></tr>
<tr><td rowspan="10">6.</td><td colspan="5">Assay
(By HPLC)</td><td rowspan="3">%ASSAY
↓</td></tr>
<tr><td rowspan="2">Area of Standard</td><td colspan="4">Area of Sample</td></tr>
<tr><td colspan="4">BATCH NO.</td></tr>
<tr><td>CAF28001</td><td>CAF28002</td><td>CAF28003</td><td rowspan="9">100.2</td><td rowspan="9">101.6</td><td rowspan="9">102.1</td></tr>
<tr><td>78655528</td><td rowspan="3">78975673</td><td rowspan="3">77406585</td><td rowspan="3">76714330</td></tr>
<tr><td>78134292</td></tr>
<tr><td>79040569</td></tr>
<tr><td>79113287</td><td rowspan="2">79118865</td><td rowspan="2">77820043</td><td rowspan="2">76348542</td></tr>
<tr><td>77585799</td></tr>
<tr><td>MEAN</td><td>78505895</td><td>79047269</td><td>77613314</td><td>76531436</td></tr>
<tr><td>Standard Deviation</td><td colspan="4">644565.12</td></tr>
<tr><td>% RSD</td><td colspan="4">0.82</td></tr>
</table>

6. Long Term Stability Study of Ozace MD-10 mg Tablet (6th- MONTH), 30°C/75%RH:

The 6th Month Long Term stability data of Ozace MD-10 mg tablet is given as following below table.

Table 2.13: Long Term Stability Study of Ozace MD-10 mg tablet are given as bellow of 6th Month.

S.NO.	PARAMETER	ANALYTICAL STASTICAL DATA
1.	Description	Yellow coloured, elongated, biconvex, scored on one side and plain on other side, Uncoated Mouth Dissolving tablet.

<table>
<tr><td>2.</td><td colspan="4">Average Weight</td><td colspan="3">169.08 mg ± 4.0 %</td></tr>
<tr><td>3.</td><td colspan="4">Disintegration Time</td><td colspan="3">28 Second</td></tr>
<tr><td>4.</td><td colspan="4">Hardness</td><td colspan="3">3.8 kg/cm^2</td></tr>
<tr><td>5.</td><td colspan="4">Friability</td><td colspan="3">0.24 %</td></tr>
<tr><td rowspan="10">6.</td><td colspan="4">Assay
(By HPLC)</td><td colspan="3">%ASSAY
↓</td></tr>
<tr><td rowspan="2">Area of Standard</td><td colspan="3">Area of Sample</td><td colspan="3" rowspan="2"></td></tr>
<tr><td colspan="3">BATCH NO.</td></tr>
<tr><td>CAF28001</td><td>CAF28002</td><td>CAF28003</td><td rowspan="6">101.8</td><td rowspan="6">101.3</td><td rowspan="6">100.9</td></tr>
<tr><td>78655528</td><td rowspan="3">77688186</td><td rowspan="3">77327187</td><td rowspan="3">78500145</td></tr>
<tr><td>78134292</td></tr>
<tr><td>79040569</td></tr>
<tr><td>79113287</td><td rowspan="2">77348522</td><td rowspan="2">77201672</td><td rowspan="2">77130032</td></tr>
<tr><td>77585799</td></tr>
<tr><td>MEAN</td><td>78505895</td><td>77518354</td><td>77264430</td><td>77815089</td></tr>
<tr><td>Standard Deviation</td><td colspan="4">644565.12</td></tr>
<tr><td>% RSD</td><td colspan="4">0.82</td></tr>
</table>

7. Long Term Stability Study of Ozace MD-10 mg Tablet (9th- MONTH), 30°C/75%RH:

The 9th Month Long Term stability data of Ozace MD-10 mg tablet is given as following below table.

Table 2.14: Long Term Stability Study of Ozace MD-10 mg tablet are given as bellow of 9th Month.

S.NO.	PARAMETER	ANALYTICAL STASTICAL DATA
1.	**Description**	Yellow coloured, elongated, biconvex, scored on one side and plain on other side, Uncoated Mouth Dissolving tablet.
2.	**Average Weight**	169.97 mg ± 4.0 %

<table>
<tr><td>3.</td><td colspan="4">Disintegration Time</td><td colspan="3">26 Second</td></tr>
<tr><td>4.</td><td colspan="4">Hardness</td><td colspan="3">3.7 kg/cm^2</td></tr>
<tr><td>5.</td><td colspan="4">Friability</td><td colspan="3">0.25 %</td></tr>
<tr><td rowspan="11">6.</td><td colspan="4">Assay
(By HPLC)</td><td colspan="3" rowspan="3">%ASSAY
↓</td></tr>
<tr><td rowspan="2">Area of Standard</td><td colspan="3">Area of Sample</td></tr>
<tr><td colspan="3">BATCH NO.</td></tr>
<tr><td>CAF28001</td><td>CAF28002</td><td>CAF28003</td><td rowspan="6">99.76</td><td rowspan="6">101.8</td><td rowspan="6">100.4</td></tr>
<tr><td>119318943</td><td rowspan="3">119083827</td><td rowspan="3">125090362</td><td rowspan="3">119301625</td></tr>
<tr><td>120287846</td></tr>
<tr><td>119534887</td></tr>
<tr><td>119871989</td><td rowspan="2">119574204</td><td rowspan="2">125277517</td><td rowspan="2">120624276</td></tr>
<tr><td>120470905</td></tr>
<tr><td>MEAN</td><td>119896914</td><td>119329016</td><td>125183940</td><td>119962951</td></tr>
<tr><td>Standard Deviation</td><td colspan="4">486833.85</td></tr>
<tr><td>% RSD</td><td colspan="4">0.41</td></tr>
</table>

CONCLUSION:

The proposed technique was simple, sensitive and reliable with accurate precision and accuracy. This approach is precise while estimating the business method barring interference of excipients and the different additives. Hence, it can be used for routine determination of Olanzapine in bulk sample. The proposed technique for stability study indicated on Accelerated and Long Term Stability Study were carryout satisfactory in condition the drug was indicating the % Assay in between the range of 100-103% that is very good range at Accelerated stability study for 6 months and Long Term Stability study for 9 Months.

ACKNOWLEDGEMENT:

Vipin Kumar Tomar (Sr. Manager, Quality Control) would like to acknowledge the support during this research article from, Psychotropic India Limited, Haridwar (U.K.), for its esteemed support and encouragement for their support and continuous encouragement and for providing the necessary facilities.

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