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Estimation of Olanzapine and Samidorphan in bulk and Pharmaceutical Dosage Form Using RP-HPL

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ABSTRACT

A new, simple, responsive, and stable RP-HPLC technique for measuring Olanzapine and Samidorphan's active pharmaceutical components was developed and validated in this study. RP-HPLC technique for the quantitative measurement of Olanzapine and Samidorphan that has been verified and has a well defined stability. Using an Inertsil ODS column with dimensions of 250x4.6 mm and a 5 micron isocratic elution with an acetonitrile/0.1 percent ortho phosphoric acid mobile phase, we developed a chromatographic method (50:50). Instrumental conditions included a stream rate of 1 ml/min and a detection absorbance of 261 nm using the photo diode array detector. To speed up the chromatographic process, an impurity-spiked solution was used instead of water. An international conference on harmonisation (ICH) set rules for validating the proposed approach, which were followed throughout validation. A regression value of R2 > 0.999 shows the linearity of the calibration charts was within the limit. In test conditions, the suggested approach is rapid, simple, practicable, and reasonably priced. For regular examination of manufacturing samples and for verifying the quality of medication samples during stability studies, it may be used.

Key words: *Olanzapine, Samidorphan, RP-HPLC, Development, Validation*

INTRODUCTION

Atypical antipsychotics like Zyprexa are used to treat schizophrenia and bipolar disorder. Olanzapine is an atypical antipsychotic [1, 2]. It may be used to treat schizophrenia [3, 4] and bipolar disorder [5] during the outset of the illness as well as to keep it under control over the long term. It may be administered orally or intramuscularly. Weight gain, mobility abnormalities [6], dizziness [7] and constipation [8] are some of the most common adverse effects. Low blood pressure [9, 10], Allergy responses [11], neuroleptic malignant syndrome (NMS) [12], excessive blood sugar [13], gynecomastia [14], erectile dysfunction [15] and delayed dyskinesia [16]. It has been shown to increase the risk of mortality in elderly patients with dementia who take it. If used late in pregnancy, there is a chance that the baby may be born with a movement abnormality that will last for some time.

Samidorphan, an opioid antagonist [17], is used to treat schizophrenia and bipolar disorder. Olanzapine-induced weight gain may be mitigated by taking samidorphan in addition to the medication. Mouth-to-mouth samidorphan is used for this purpose. The FDA rejected buprenorphine/samidorphan for the treatment of major depressive disorder because to inadequate proof of efficacy. There are several possible side effects of samidorphan, including drowsiness [18] and gastrointestinal issues [19]. Researchers at Alkermes [20] have looked at the potential of samidorphan to treat alcoholism [21] and cocaine addiction [22], finding that it has comparable effectiveness to naltrexone [23] while having less adverse effects.

MATERIALS AND METHODS

Chemicals

Merck India Ltd, Mumbai, India, supplied acetonitrile, HPLC-grade ortho phosphoric acid, and water. Dr. Reddy's laboratory, Hyderabad, supplied APIs of Olanzapine and Samidorphan standards.

The instrumentation

This research made use of a Waters Alliance liquid chromatography (model 2695) supervised by a data processing system called empower 2.0 and a light diode array detector (model 2998).

Method optimization

Different isocratic and gradient phosphate buffer/acetonitrile mobile phase ratios were examined in order to optimise the chromatographic circumstances. Each experiment, however, used a different mobile phase composition to achieve better resolution and longer acceptable retention durations. The 0.1 percent ortho phosphoric acid buffer and acetonitrile with isocratic elution was used because it resulted in a greater response from active medicinal components. ˈPhenomenal and amino - inertsil ODS columns as well as various stationary phases were tested during process optimization″.With the inertsil ODS column, which measures 250 x 4.6mm and a PDA detector set at 5, the peak shapes obtained from these tests were satisfactory. Obtaining a high level of sensitivity necessitated setting the flow rate of the mobile phase to 261nm. Retention times for Olanzapine and Samidorphan were around 3.013 and 7.267 minutes, respectively, with a tailing factor of 1.04 and 1.01. Olanzapine and Samidorphan produced 3102 and 6637 theoretical plates, respectively, indicating that the column was a success. Each of the six injections had a relative standard deviation of 0.23 percent to 0.61 percent. By all accounts, the strategy put forward seems to be quite exact. The approach devised was validated in accordance with ICH standards.

Validation procedure [24-28]

The International Conference on Harmonisation's Q2 (R1) criteria were used to evaluate the analysis's precision, specificity, accuracy, and linearity.

Preparation of buffer

In order to purify 1 Lt of HPLC water, 1 ml of formic acid was dissolved in 0.45 filter paper and the solution was filtered.

Chromatographic conditions

On a reverse phase HPLC system, isocratic elution mode was used with an acetonitrile and ortho-phsophoric acid mobile phase, inertsil ODS (250x4.6mm, 5 µm) column at 1 ml/min stream rate.

Preparation of the standard stock solution

Sonicate for 10 minutes to completely dissolve the 50 mg Olanzapine and the 50 mg Samidorphan in the 100 ml volumetric flask, then add the rest of the required amount of diluent to make up the 70 ml required for the creation of a standard stock solution.

The typical stock solution is used to dilute 1 ml of the sample in a volumetric flask of 10 ml.

Preparation of sample solution

Sonicate for 10 minutes to dissolve Olanzapine and Samidorphan sample in a 100 ml volumetric flask with 70 ml diluents and then add the remaining diluents to get the volume to the mark. A 0.45 mm nylon syringe is used to filter this solution into a device in a vial.

RESULTS AND DISCUSSION

The most difficult part of developing a new approach was separating active pharmaceutical components. The chromatographic conditions were fine-tuned in order to get the best results possible.

System suitability

A system suitability chromatogram is shown in **Figure 1** together with the injection, USP tailing and plate count values stated in the standard solution.

Table 1. Results of system suitability

Parameters of suitability	Acceptance criteria	Drug name	
		Olanzapine	Samidorphan
USP Plate Count	NLT 2000	3102	6637
USP Tailing	NMT 2.0	1.04	1.01
USP Resolution	NLT 2.0	-	10.32
% RSD	NMT 2.0	0.23	0.61

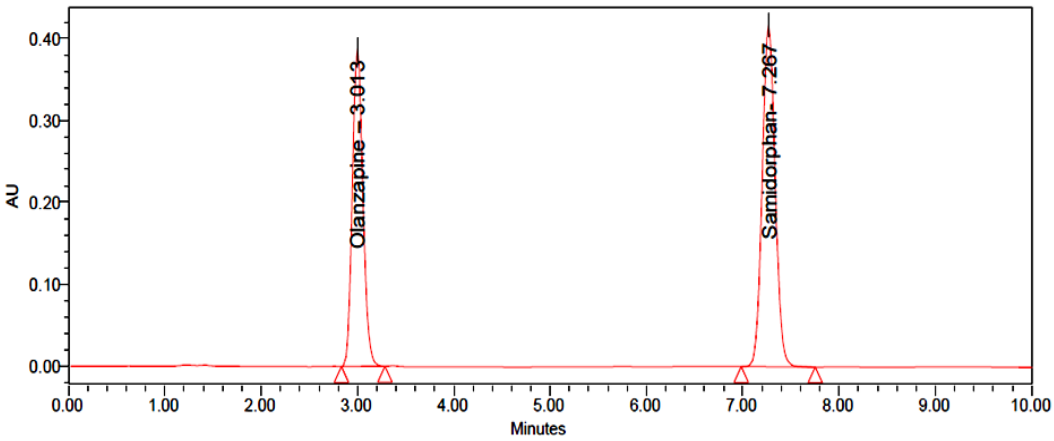


Figure 1. Chromatogram of standard

Specificity

The interference was examined by analysing each of the test solutions separately, including the placebo, the sample, and the standard. The figure below indicates that the active components and their excipients were clearly separated from the blank and did not interfere with the main peak. As a result, the procedure is particular, as seen in **Figure 2** by a blank chromatogram.

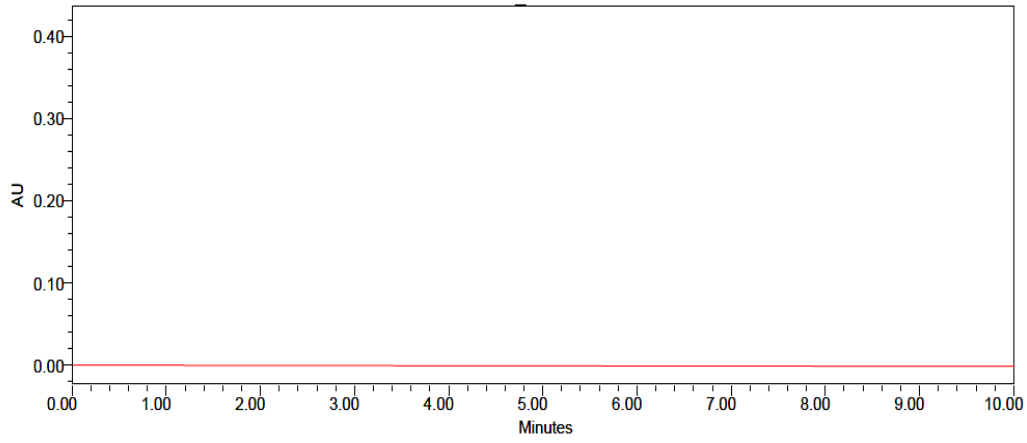


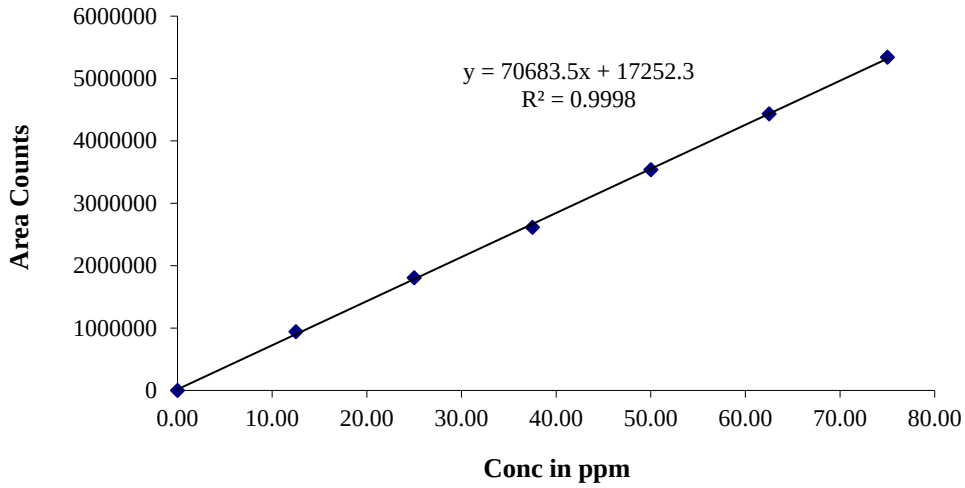
Figure 2. Chromatogram of blank

Linearity

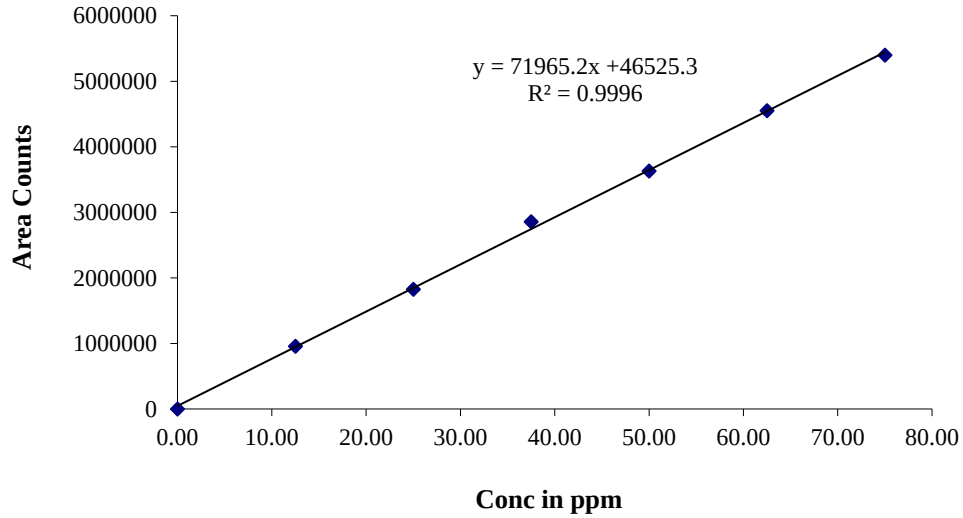
Olanzapine and Samidorphan were shown to have linearity peaks with areas of 10, 25, 50, 100, 125, and 150 percent, respectively, when tested at various doses. Olanzapine linearity was tested between 15 and 225 µg/ml and Samidorphan linearity was tested between 4 and 60 µg/ml. In every case, there was a correlation coefficient larger than 0.999 Calibration plots are given in **Figure 3** and linearity findings are provided in **Table 2**.

Table 2. Linearity results of Olanzapine and Samidorphan

S.no	Conc (µg/ml)	OlanzapineResponse	Conc.µg/ml	SamidorphanResponse
1	12.50	941624	12.50	956383
2	25.00	1806984	25.00	1824638
3	37.50	2613647	37.50	2856572
4	50.00	3538351	50.00	3630360
5	62.50	4432646	62.50	4550920
6	75.00	5341942	75.00	5397679
Correl coef		0.9998		0.99961
Slope		70683.53		71965.24
intercept		17252.32		46525.32



a)



b)

Figure 3. Calibration plots of (A) Olanzapine (B) Samidorphan

Accuracy

Analyzing active pharma component sample solution at 50, 100, and 150 percent concentrations at a specific limit was done in triplicate in this approach. It was determined that percentage recoveries were within the acceptable range. The new method's precision and dependability have been proven. **Tables 3-5** provide the findings.

Table 3. Accuracy results

S. No	% Level	Olanzapine % Recovery	Samidorphan % Recovery
1	50	101.2	100.1
2	100	99.9	100.2
3	150	100.6	100.1

Intraday precision

Olanzapine (150 µg/ml) and Samidorphan (40 µg/ml) were tested in six duplicates on the same day. Mean, standard deviation, and percent RSD were computed using peak regions. **Table 4** shows the outcomes of this study.

Table 4. Intraday precision outcomes

	Olanzapine		Samidorphan	
S.No	Conc.(µg/ml)	Response	Conc.(µg/ml)	Response
1	50	3550571	50	3625648
2		3579840		3601256
3		3548354		3648642
4		3514361		3635143
5		3523214		3670474
6		3566521		3684123

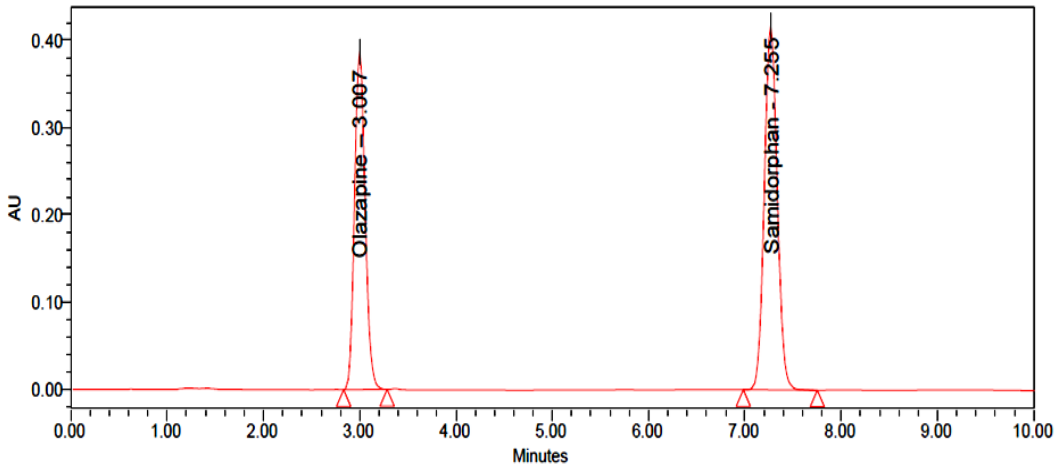


Figure 4. Chromatogram of sample

Inter-day precision

Intermediate precision is another name for this level of accuracy. For the purpose of this study, Olanzapine and Samidorphan were tested in six separate samples over the course of one day. The RSD values were discovered to be less than 2%, and the percentage assay values were also found to be near to 100%. **Table 5** summarises the findings of this study.

Table 5. Inter-day outcomes of accuracy of Olanzapine and Samidorphan

	Olanzapine		Samidorphan	
S.No.	Conc.(µg/ml)	Response	Conc.(µg/ml)	Response
1	50	3592123	50	3637654
2		3548154		3593216
3		3567854		3696241
4		3533215		3687548
5		3578974		3671452
6		3558820		3628543

LOD and LOQ

Olanzapine has a LOD of 1.6 µg/ml and a s/n of 6, whereas Samidorphan has a LOD of 1.6 µg/ml and a s/n of 6. Both Olanzapine and Samidorphan have LOQ concentrations of 5 µg/ml and s/n values of 25. The procedure has been validated in accordance with ICH standards.

Table 6. LOD and LOQ data

Olanzapine				**Samidorphan**			
LOD		**LOQ**		**LOD**		**LOQ**	
Conc.	s/n	Conc.	s/n	Conc.	s/n	Conc.	s/n
1.6 µg/ml	6	5 µg/ml	25	1.6µg/ml	6	5µg/ml	25

Robustness

Stream rate and the quantity of organic material in the carrier phase were two of the many factors that were put through their paces. Olanzapine and Samidorphan were shown to have robustness that was within the limit in **Table 7**.

Table 7. Robustness results of Olanzapine and Samidorphan

Parameter name	**% RSD**	
	Olanzapine	**Samidorphan**
FM (0.8 ml/min)	0.72	0.56
FP (1.2 ml/min)	0.90	0.81
Organic minus (45:55)	0.92	1.1
Organic plus (55:45)	1.01	0.44

Stability

Room temperature and RT were used for the standard and sample solutions, respectively. Pumping these solutions into the apparatus, the percentage of divergence from initial to 24 h was calculated. There was no substantial variation seen and it was proven that the solutions remained stable up to 24 hours. Olanzapine and Samidorphan medicines have no influence on storage conditions. In the following, you'll find the findings in **Table 8**.

Table 8. Stability RT results of Olanzapine and Samidorphan

Stability	**Olanzapine**		**Samidorphan**	
	Purity	**% of deviation**	**Purity**	**% of deviation**
Initial	100	0.00	100	0.00
6 h	99.7	-0.30	99.8	-0.20
12 h	99.5	-0.50	99.6	-0.40
18 h	99.4	-0.60	99.3	-0.70
24 h	99.1	-0.90	98.9	-1.10

Degradation studies

Samidorphan and Olanzapine samples were put through a series of degrading settings to see whether they could be broken down in any way. Forced degradation studies have been conducted to determine whether the procedure is appropriate for items that have been degraded. As a result of these research, formulations are often tweaked to minimise possible instabilities because of the information they give.

Acid degradation

Olanzapine degraded at a 12.2 percent rate in 1N HCl, whereas Samidorphan degraded at a 10.7 percent rate.

Alkali degradation

Olanzapine and Samidorphan were degraded at a concentration of 1N NaOH, which resulted in 10.8 and 11.5 percent degradation, respectively.

Peroxide degradation

Olanzapine and Samidorphan both degraded at a rate of 13.7% and 15.1%, respectively, when exposed to a solution containing 20 percent hydrogen peroxide.

Reduction degradation

There was a 10.4 percent Olanzapine degradation and an 11.9 percent Samidorphan decrease in the reduced degradation.

Thermal degradation

5.9 percent of Olanzapine and 14.1% of Samidorphan were destroyed in the thermal degradation of the sample.

Degradation of hydrolysis

Olanzapine and Samidorphan were reduced to 0.3 percent and 0.1 percent, respectively, in hydrolysis degradation. **Table 9** contains the outcomes of all degradations.

Table 9. Degradation results of Olanzapine and Samidorphan

Degradation condition	Olanzapine		Samidorphan	
	% assay	%Deg	% assay	% Deg
Acid deg	87.8	12.2	89.3	10.7
Alkali deg	89.2	10.8	88.5	11.5
Peroxide deg	86.3	13.7	84.9	15.1
Reduction deg	89.6	10.4	88.1	11.9
Thermal deg	94.1	5.9	85.9	14.1
Hydrolysis deg	99.7	0.3	99.9	0.1

CONCLUSION

Samidorphan and olanzapine concentrations may be determined with the use of the well-defined isocratic RP-HPLC method. Stress-induced degradation products and their active pharmaceutical components were well separated and peaks were well resolved from each other, showing that the approach is rapid, simple, practicable, and economical under assay circumstances. A new approach for analysing manufacturing samples and checking the quality of medicine samples during stability studies was developed during stability testing.

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CONFLICT OF INTEREST : None

FINANCIAL SUPPORT : None

ETHICS STATEMENT : None

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