



ISSN: 0976-3031

Available Online at <http://www.recentscientific.com>

CODEN: IJRSFP (USA)

International Journal of Recent Scientific Research
Vol. 8, Issue, 4, pp. 16559-16562, April, 2017

**International Journal of
Recent Scientific
Research**

DOI: 10.24327/IJRSR

Research Article

DEVELOPMENT AND VALIDATION OF SPECTROSCOPIC METHOD FOR SIMULTANEOUS ESTIMATION OF PALIPERIDONE AND OLANZAPINE IN SYNTHETIC MIXTURE

Farzana I Ghanchivhora¹, Jignesh S. Shah² and Maheswari D. M³

Department of Quality Assurance, L.J. Institute of Pharmacy, Ahmedabad, Gujarat

DOI: <http://dx.doi.org/10.24327/ijrsr.2017.0804.0171>

ARTICLE INFO

Article History:

Received 15th January, 2017
Received in revised form 25th
February, 2017
Accepted 23rd March, 2017
Published online 28th April, 2017

Key Words:

Paliperidone, Olanzapine, UV
Spectrophotometric method

ABSTRACT

A simple, specific, accurate, precise and economical spectrophotometric method has been developed for the estimation of Paliperidone and Olanzapine in synthetic mixture. The absorption maxima of the drugs were found to be 269nm and 259nm for Paliperidone and Olanzapine respectively. Paliperidone and Olanzapine obeyed Beer's law in the concentration range 3-18 µg/ml and 2-12 µg/ml respectively. Different analytical parameter such as linearity, precision, accuracy, limit of detection (LOD), limit of quantitation (LOQ), were determined as per ICH guidelines. Hence, the developed method can be used quality control analysis.

Copyright © Farzana I Ghanchivhora., Jignesh S. Shah and Maheswari D. M, 2017, this is an open-access article distributed under the terms of the Creative Commons Attribution License, which permits unrestricted use, distribution and reproduction in any medium, provided the original work is properly cited.

INTRODUCTION

Paliperidone chemically 3-[2-[4-(6-fluoro-1,2-benzoxazol-3-yl)piperidin-1-yl]ethyl]-9-hydroxy-2-methyl-6,7,8,9-tetrahydropyrido[1,2-a]pyrimidin-4-one. Paliperidone is a primary active metabolite of the older antipsychotic risperidone. The drug's therapeutic activity in schizophrenia is mediated through a combination of central dopamine Type 2 (D2) and serotonin Type 2 (5HT2A) receptor antagonism. Paliperidone is also active as an antagonist at alpha 1 and alpha 2 adrenergic receptors and H1 histaminergic receptors.

Olanzapine chemically 2-Methyl-4-(4-methyl-1-piperazinyl)-10H-thieno [2,3-b][1,5]benzodiazepine. Olanzapine is a single capsule containing the atypical antipsychotic olanzapine and the selective serotonin reuptake inhibitor (SSRI). Olanzapine is primarily used for the depressive episodes of bipolar I disorder as well as treatment resistant depression.

A synthetic mixture of Paliperidone and Olanzapine is the synergistic effect was observed by improving psychotic symptoms. Literature survey several method have been developed for the determination of Paliperidone and Olanzapine each single formulation. The work is the UV spectroscopic method of Paliperidone and Olanzapine in synthetic mixture.

Structure

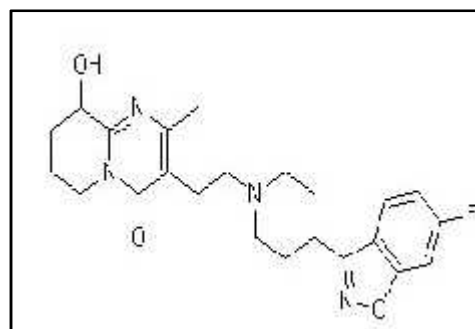


Fig 1 Chemical structure of Paliperidone

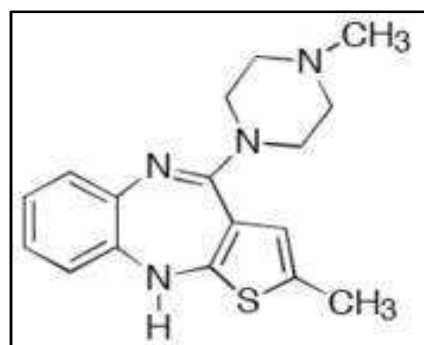


Fig 2 Chemical structure of Olanzapine

*Corresponding author: **Farzana I Ghanchivhora**

Department of Quality Assurance, L.J. Institute of Pharmacy, Ahmedabad, Gujarat

MATREIALS AND METHODS

Instrumentation

A double beam UV-VIS spectrophotometer (UV- 1800, Shimadzu) connected to computer loaded with spectra manager software UV probe was employed with spectral band width of 1nm and wavelength accuracy of $\pm 0.3\text{nm}$ with a pair of 10 mm matched quartz cells. All weights were taken on electronic balance.

Chemicals and reagents

Methanol used as diluent. Drug sample of Paliperidone and Olanzapine was given as a gift sample by Intas pharmaceutical ltd and cadila pharmaceutical ltd. Tablets of Paliperidone and Olanzapine were produced from local market.

Selection of a Solvent

Methanol was selected as solvent for studying spectral characteristic of drug.

Preparation of standard stock solution

Preparation of standard stock solution of Paliperidone (100 $\mu\text{g/ml}$):

Accurately weigh 10 mg of Paliperidone was transferred into a 100 ml volumetric flask and diluted with Methanol.

Preparation of standard stock solution of Olanzapine (100 $\mu\text{g/ml}$):

Accurately weigh 10 mg of Olanzapine was transferred into a 100 ml volumetric flask and diluted with Methanol.

Preparation of Calibration curve

Calibration curve of Paliperidone (3-18 $\mu\text{g/ml}$):

Aliquots of stock solution of Paliperidone (100 $\mu\text{g/ml}$) (0.3, 0.6, 0.9, 1.2, 1.5 and 1.8 ml) was pipetted out in five different 10 ml volumetric flask and made up to mark with methanol which will give 3, 6, 9, 12, 15 and 18 $\mu\text{g/ml}$ respectively. Absorbance of each solution was measured at 269 nm using methanol as blank. Graph of Absorbance Vs Concentration was plotted.

Calibration curve of Olanzapine (2-12 $\mu\text{g/ml}$):

Aliquots of stock solution of Olanzapine (100 $\mu\text{g/ml}$) (0.2, 0.4, 0.6, 0.8, 1.0 and 1.2 ml) was pipetted out in five different 10 ml volumetric flask and made up to mark with methanol which will give 2, 4, 6, 8, 10 and 12 $\mu\text{g/ml}$ respectively. Absorbance of each solution was measured at 259 nm using methanol as blank. Graph of Absorbance Vs Concentration was plotted.

Procedure

Selection of Analytical Wavelength

Standard 3-18 $\mu\text{g/ml}$ solution of Paliperidone and 2-12 $\mu\text{g/ml}$ solution of Olanzapine were prepared in methanol by appropriate dilution and spectrum was recorded between 200-400 nm. All zero order spectrum (D_0) were converted to first derivative spectrum (D_1) using delta lambda 2.0 and scaling factor 10. The overlain first derivative spectrums of Paliperidone and Olanzapine at different concentration were

recorded. The zero crossing point (ZCP) of Paliperidone and Olanzapine found to be 269 nm and 259 nm.

METHOD VALIDATION

Linearity

Linearity evaluates the analytical procedure's ability (within a given range) to obtain a response that is directly to the concentration (amount) of analyte standard. If the method is linear, the test results are directly, proportional to the concentration of analyte in samples within a given range. A calibration curve is prepared by plotting absorbance (Y) as a function of concentration (X) which procedures a linear curve with correlation equation.

$$Y = mX + c$$

Coefficient of determination (r^2) should be 0.9999.

Range

Range is the interval between the upper and lower concentration (amounts) of analyte in the sample (including these concentrations) for which it has been demonstrated that the analytical procedure has a suitable level of precision, accuracy and linearity.

Coefficient of determination (r^2) should be 0.9998.

Accuracy (recovery)

Accuracy expresses the closeness agreement between the value found and the value that is accepted as either a conventional true value or an accepted reference value. It may often be expressed as the recovery by the assay of known, added amounts of analyte.

Coefficient of determination (r^2) should be greater than 0.9998.

Precision

Validation of tests for assay and for quantitative determination of impurities includes an investigation of precision.

Repeatability

Repeatability evaluates the variation by a single analyst on a single instrument. Repeatability does not distinguish between variation from the instrument or system alone and from the sample preparation process. Repeatability is performed by analyzing multiple replicates of an assay composite sample using the analytical method. The recovery value is calculated and reported for each value.

Intermediate Precision

Intermediate precision refers to variation within a laboratory as with in different days, with different instruments, by different analysts, and so forth intermediate precision was formally known as ruggedness. A statistical comparison is made to the first analyst's results.

$$SD = \sqrt{\frac{\sum (x - \bar{x})^2}{N - 1}}$$

X_i = individual measurement in a set

X = arithmetic mean of the set and

N = number of replicates taken in the set

$RSD = SD/X$

% RSD or coefficient of variance (CV) is expressed as

$$\%RSD = CV = SD/X*100$$

The % RSD of the assay/recovery values generated by a single analyst should not be greater than 2.0%.

The %RSD of the combined assay/recovery values generated by both analyst, over both analyst should not be greater than 2.0%.

The %RSD of the related compounds recovery value should not be greater than 15%.

Detection limit

The detection limit (DL or limit of detection LOD) of an individual procedure is the lowest of analyte in a sample that can be detected but not necessarily quantitated as an exact value.

The detection limit (DL) may be expressed as:

$$DL = 3.3 * S$$

Where, S= the slope of calibration curve

= Standard deviation of blank reading or intercepts of calibration curve

Quantitation limit

The quantitation limit (QL or limit of detection LOQ) of an individual procedure is the lowest amount of analyte in a sample that can be quantitatively determined with suitable precision and accuracy.

The quantitation limit (QL) may be expressed as:

$$QL = 10 * S$$

Where, S= the slope of calibration curve

= Standard deviation of blank reading or intercepts of calibration curve

RESULT AND DISCUSSION

A reliable first order derivative spectrophotometric method was developed for simultaneous estimation of Paliperidone and Olanzapine in sythetic mixture by UV spectrophotometry. Beer’s law was obeyed in concentration range of 3-18 µg/ml for Paliperidone and 2-12 µg/ml for Olanzapine at 269 nm and 259 nm wavelengths, respectively. The correlation coefficient Paliperidone and Olanzapine was found to be R₂= 0.998 and 0.999. The mean % recoveries were found to be in the range of 99.2%-101.99% and 99%-102%, respectively. The LOD and LOQ were 0.2131 µg/ml and 0.645 µg/ml of Paliperidone and 0.218 µg/ml and 0.662 µg/ml of Olanzapine, respectively. The proposed method was precise, accurate and reproducible and acceptable recovery of the analyses, which can be applied for the analysis of Paliperidone and Olanzapine in sythetic mixture.

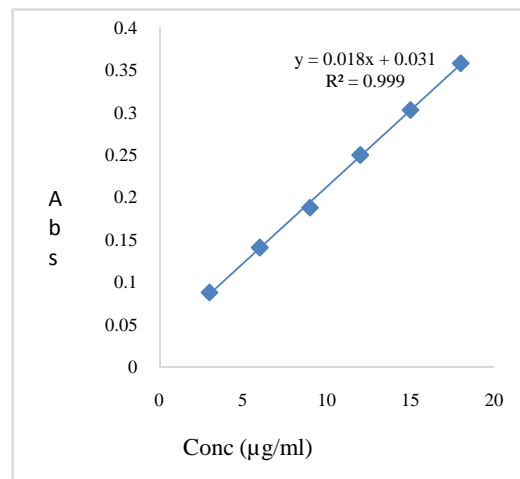
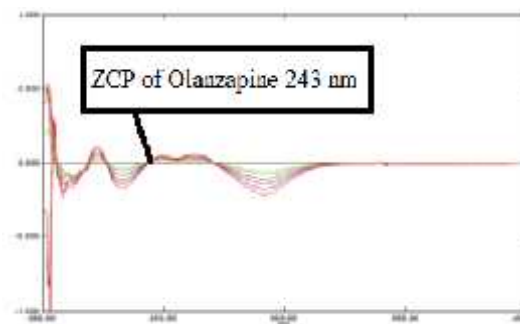


Fig Calibration curve of Paliperidone

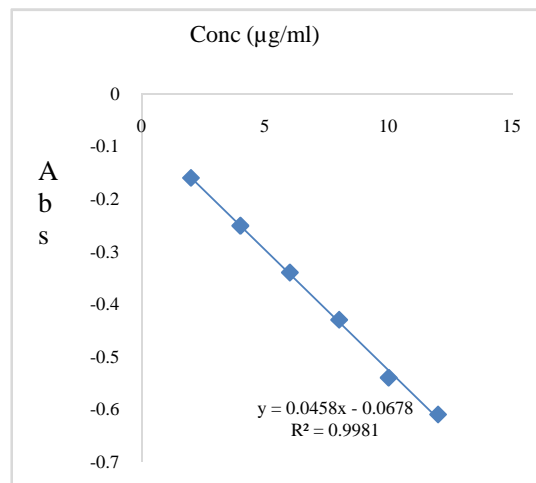


Fig Calibration curve of Olanzapine

Table no 1 Optical characteristics

Parameter	Paliperidone	Olanzapine
Beer’s law limit	3-18 µg/ml	2-12 µg/ml
Regression equation	0.0181x + 0.0315	-0.0458x - 0.0678
Slope (m)	0.0181	-0.0458
Intercept (c)	0.0315	0.0678
Correlation coefficient	0.999	0.998

Table no 2 Results of accuracy

Name of drug	% level of recovery	Test amount	Amount taken	Total amt of drug	Amount recovered	% Recovery
Paliperidone	50	3	6	9	8.9	98.89
	100	6	6	12	11.8	98.34
	150	9	6	15	14.9	99.34
Olanzapine	50	2	4	6	5.9	98.33
	100	4	4	8	7.9	98.75
	150	6	4	10	9.9	99

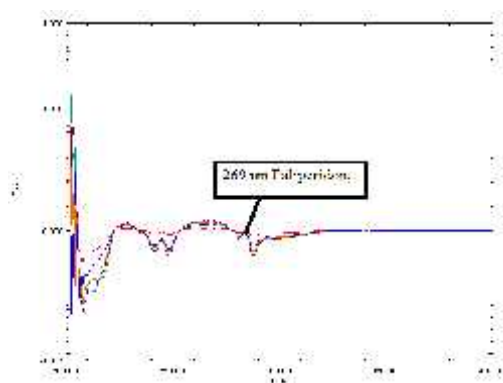


Table no 3 Repeatability, Intra-day, Inter-day precision of Paliperidone and Olanzapine

Drug	Conc	Avg ± sd	% Rsd
Repeatability (n=6)			
Paliperidone	6	0.1435±0.001366	0.952398
Olanzapine	4	0.257±0.003545	1.37936
Intra-day precision (n=3) [Paliperidone]			
Drug	Conc	Avg± sd	%Rsd
Paliperidone	6	0.142333±0.001155	0.811265
	12	0.251667±0.001528	0.606964
	18	0.359667±0.001528	0.424706
Olanzapine	4	0.254±0.003	1.1811
	8	0.43333±0.003055	0.71501
	12	0.61367±0.003215	0.52383
Inter-day precision (n=3)[Olanzapine]			
Drug	Conc	Avg	% Rsd
Paliperidone	6	0.142±0.001	0.704225
	12	0.251333±0.001528	0.607769
	18	0.36±0.002	0.55555
Olanzapine	4	-0.25367±0.003055	1.20436
	8	-0.4333±0.003055	0.70501
	12	-0.6138±0.003215	0.5238

Table no 4 Limit of detection (LOD) and Limit of quantitation (LOQ)

Parameter	LOD	LOQ
Paliperidone (µg/ml)	0.2131	0.645
Olanzapine (µg/ml)	0.218	0.662

Table no 5 Summary of validation parameter

Sr no	Parameters	Paliperidone	Olanzapine
1	Linearity Range (µg /ml)	3-18 µg/ml	2-12 µg/ml
2	Regression Line Equation (y = mx + c)	0.0181x + 0.0315	-0.0458x - 0.0678
3	Correlation coefficient (R ²)	0.999	0.998
4	Intraday precision (%RSD, n=3)	0.606964	0.71501
5	Interday precision (%RSD, n=3)	0.5554-0.704225	0.5238 - 1.20436
6	Repeatability (%RSD, n=6)	0.952398	1.37936
7	LOD (µg /ml)	0.2131	0.218
8	LOQ (µg /ml)	0.645	0.662
9	% Recovery study (n=3)	98.34	97.5

CONCLUSION

A simple accurate and precise UV spectrophotometric method has been developed for the estimation of Paliperidone and Olanzapine in synthetic mixture. It has advantage that it eliminates the spectral interference from one of the two drugs while estimating the other drug at selected wavelength.

Acknowledgement

We are heartly thankful to Dr. K. Pundarikakshudu, Director of L. J. Institute of Pharmacy, Ahmedabad for providing all the facilities and the valuable guidance during the research work.

References

- Goyal R.K., Mehta A. A., Balaraman R., Derasari and Gandhi's elements of pharmacology, 7th edition, B.S.Shah Prakashan pharmacology, 7th the edition, B.S.Shah prakashan Publication, 2007-2008, pp. 450, 455-457.
- Drug.com, "Side effects and dose of Olanzapine" www.drugs.com/olanzapine.html
- Drug bank, "Description, physicochemical properties, pharmacology, overdose, pharmacokinetics, interaction and marketed formulation of Olanzapine", www.drugbank.ca/drugs/DB0065.
- Medline plus <http://medlineplus.gov>
- ICH, Q2 (R1) Validation of analytical procedures: Text and Methodology International Conference on Harmonization, IFPMA, Geneva, Switzerland, 2005
- Chatwal GR., and Anand S. Instrumental method of Chemical Analysis; 5th Edition; Himalaya Publishing House, New Delhi, 2002, pp20149-2.184, 2.624-2.639.
- Skoog DA, Holler JA. And Nieman TA. Principle of Instrumental Analysis; 5th Edn; Thomson Asia Pte Limited, pp 300-328, 725-744.
- Willard HH., Merritt LL., Dean JA., and Settle JR., Instrumental Method of Analysis; 7th Edn; CBS Publisher & Distributors, New Delhi, pp 177-178, 580, 640.

How to cite this article:

Farzana I Ghanchivhora., Jignesh S. Shah and Maheswari D. M.2017, Development And Validation of Spectroscopic Method For Simultaneous Estimation Of Paliperidone And Olanzapine In Syentetic Mixture. *Int J Recent Sci Res.* 8(4), pp. 16559-16562. DOI: <http://dx.doi.org/10.24327/ijrsr.2017.0804.0171>
