Asian Journal of Pharmaceutical and Health Sciences
www.ajphs.com

An ecofriendly novel spectrophotometric estimation and validation of paliperidone in bulk drug and their dosage forms by mixed hydrotropic solubilisation method

Remi S L*[1] , Joyamma Varkey[2]

1 College of Pharmaceutical Sciences, Govt. Medical College, Thiruvananthapuram, Kerala, India.
2 TD Government Medical college, Alappuzha, Kerala, India.

ARTICLE HISTORY

Received: 06.09.2018

Accepted: 13.11.2018

Available online: 31.12.2018

Keywords:

Paliperidone, Eco-friendly, Mixed hydrotropy

***Corresponding author:**

Email : remisanthosh@yahoo.com
Phone : +91-9497692630

ABSTRACT

A novel, simple, safe, accurate and reproducible UV spectrophotometric method was developed using a hydrotropic blend of 20% sodium benzoate and 20% Niacinamide for the estimation of poorly water soluble drug Paliperidone in bulk and pharmaceutical dosage form. There were more than 87 fold solubility enhanced in hydrotropic blend as compared with distilled water. The Paliperidone shows the maximum absorbance at 286nm. At this wavelength hydrotropic agents and other tablet excipients do not shows any significant interference in the spectrophotometric assay. The developed method was found to be linear in the range of 10-50 µg/ml with correlation coefficient (r2) of 0.9990. The mean percent label claims of tablets of Paliperidone in two marketed formulation I and formulation II estimated by the proposed method was found to be 99.48 + 0.292 and 98.01 + 0.326 respectively. The developed method was validated according to ICH guidelines and values of accuracy, precision and other statistical analysis were found to be in good accordance with the prescribed values.

INTRODUCTION

Paliperidone is a long acting antipsychotic agent for the treatment of schizophrenia.Paliperidone(fig1) is chemically (RS)-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 [1] is the major active metabolite of Risperidone. The therapeutic activity of Paliperidone in schizophrenia is mediated through a combination of central dopamine type 2 (D_2) and serotonin type 2 (5HT2A) receptors and antagonism. Mixed hydrotropic solubilisation technique[2]is the phenomenon used to increase the solubility of poorly water soluble drugs in aqueous solution containing blends of hydrotropic agents, which give synergistic enhancement on solubility and reduce the concentration of each individual hydrotropic agents.Sodium salicylate, Sodium benzoate, Urea, Nicotinamide, Sodium citrate, Sodium acetate, Sodium caprylate etc. are the most common examples of hydrotropic agents utilized to increase the water solubility. Maheshwari[3-4] has analyzed various poorly water soluble drugs using hydrotropic solubilization phenomenon. Usually various costlier and toxic organic solvents have been employed for the solubilization of poorly water soluble drugs to carry out spectrophotometric analysis. Hydrotropic solution may be the proper choice to preclude the uses of organic solvents. A few HPLC, HPTLC and Spectrophotometric methods[5-9] have been reported for the estimation of Paliperidone. There was more than 87 fold enhancement in the solubility of Paliperidone in hydrotropic blend of 20% sodium benzoate and 20% Niacinamide. The primary objective of the present investigation was to employ the hydrotropic solution to extract the drug from the dosage form and precludes the use of corrosive organic solvents.

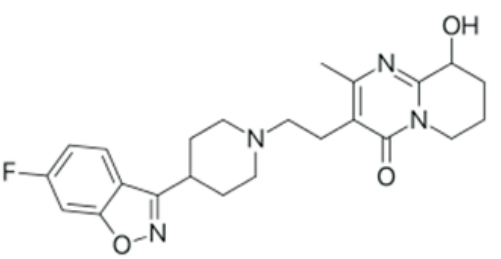

Fig. 1 : Structure of Paliperidone

MATERIALS AND METHODS

INSTRUMENTS

Spectrophotometric analysis was carried out by using a double beam UV-Visible spectrophotometer (JASCO, V-560 model) with 1cm quartz cells and Schimadzu AT X 224 weighing balance.

REAGENTS AND CHEMICALS

Analytical pure sample of Paliperdone was supplied as gift sample from Unichem Laboratories Ltd, Goa. Sodium benzoate and Niacinamide were obtained from Merck Chemical Division, Mumbai. Reverse Osmosis water was used for the study. Tablets of Paliperidone (Palido-OD 6mg, Torrent pharmaceuticals Ltd and Palivega 6mg, Zydus Cadila Health Care Ltd) were purchased from local market.

METHODS

PRELIMINARY SOLUBILITY STUDY OF THE DRUG

An excess amount of drug was added to screw capped 30ml glass vials containing different aqueous systems viz. Distilled water, different combinations of hydrotropic agent. The vials were shaken mechanically for 12 hrs at 28± 1°c in a mechanical shaker. These solutions were allowed to equilibrate for next 24 hrs and then centrifuged for 5min at 2000 r pm. The supernatant liquid was taken and filtered through whatman filter paper #41 and after appropriate dilution analyzed spectrophotometrically against corresponding reagent blank. After analysis it was found that the enhancement in the solubility of Paliperidone was more than 87 folds in a mixture of 20% solution of Sodium benzoate and 20 % Niacinamide as compared to solubility studies in other hydrotropic solutions. This enhancement in solubility is due to the hydrotropic solubilization phenomenon.

SELECTION OF HYDROTROPIC AGENT

- Paliperidone was scanned in hydrotropic solution in the spectrum mode over the UV range (200-400nm) and blend of 20% Sodium Benzoate and 20% Niacinamide were found to be most appropriate hydrotropic agent because
- Paliperidone shows 87 fold enhancement of solubility in hydrotropic blend.
- Paliperidone is stable in hydrotropic agent and also exhibit good spectral characteristics in it.
- Sodium benzoate and Niacinamide do not interfere at 286nm (λ-max of paliperidone).

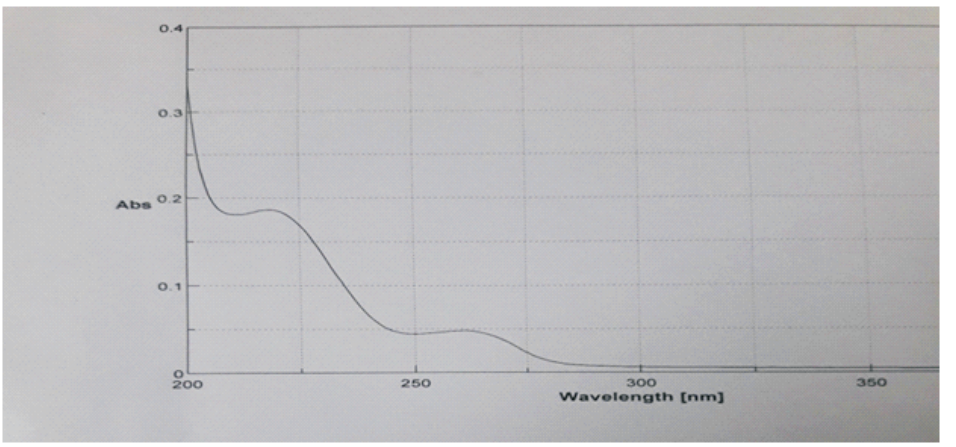

Fig. 2 : Spectra of Sodium benzoate and Niacinamide

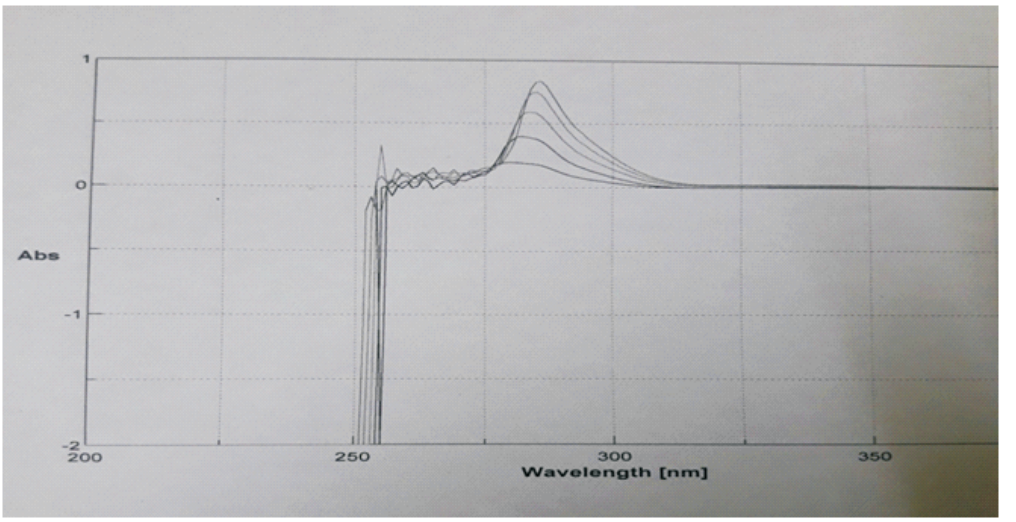

Fig. 3 : Overlay Spectrum of Paliperidone in sodium benzoate and Niacinamide

PREPARATION OF CALIBRATION CURVE

Accurately weighed 50 mg of standard Paliperidone were transferred in to 50ml volumetric flask containing 20 ml of mixed hydrotropic solution of 20% sodium benzoate and Niacinamide. Shake well and then diluted up to 50ml with distilled water. The standard solution (1000 µg/ml) was further diluted with distilled water to obtain 10,20,30,40 and 50 µg/ml. The absorbance measurements were carried out at 286nm against respective reagent blank prepared in the same manner omitting the drug. The calibration curve was prepared by plotting absorbances against concentrations (fig 4) and the data is given in (table1and 2)

Table 1: Linearity of Paliperidone at λmax 286nm in mixed

Standard conc (µg/ml) 0	Rep-1 0	Rep-2 0	Rep-3 0	Rep-4 0	Rep-5 0	Rep-6 0
10	0.19697	0.19692	o.19688	0.19693	0.19685	0.1969
20	0.39934	0.39930	0.39929	0.39936	0.39946	0.39935
30	0.59160	0.59158	0.59156	0.59164	0.59172	0.59162
40	0.78996	0.78999	0.79006	0.78994	0.78995	0.78998
50	0.94898	0.94896	0.94900	0.94904	0.94897	0.94899

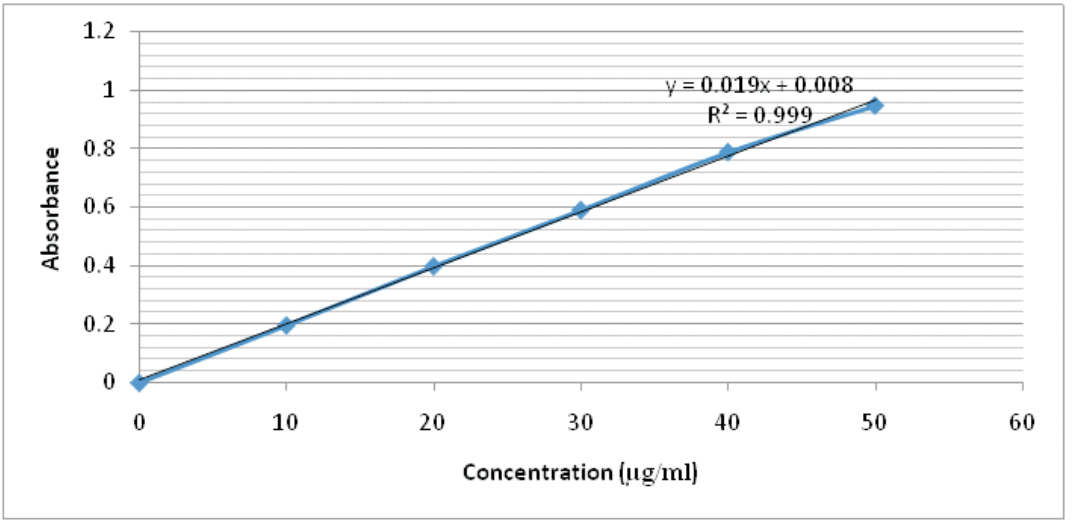

Fig. 4 : Calibration curve of Paliperidone

Table 2: Optical characteristics and linearity data of Paliperidone in mixed hydrotropic agents

Sl No	Parameter	values
1	Working λ	286nm
2	Beers law limit (µg/ml)	10-50
3	Correlation coefficient (r^2)	0.9990
4	Slope (m)*	0.019
5	Intercept (c)*	0.008
6	Number of samples (n)	25

Table 3: Result of Tablet Analysis

Amt of drug claimed (mg)	Tablet analysis using 20% sodium acetate and 20% Niacinamide as hydrotropic agent							
	Amount of drug found (mg)				Percentage estimated in formulation			
	Palido OD		Palivega		Palido OD		Palivega	
	R-1	R-11	R-1	R-11	R-1	R-11	R-1	R-11
6	5.98	5.96	5.90	5.89	99.72	99.40	98.32	98.27
6	5.95	5.99	5.87	5.85	99.18	99.83	97.97	97.47
6	5.97	5.94	5.88	5.86	99.65	99.13	98.15	97.77

ANALYSIS OF TABLET FORMULATION

Two marketed formulations Palido OD (Torrent pharmaceutical Ltd.), Palivega (Zydus Cadila Health Care Ltd) were selected for tablet analysis. Each tablet containing 6 mg Paliperidone.Twenty tablets were accurately weighed and average weight was determined and ground to fine powder. An accurately weighed quantity of powder equivalent to 50 mg of Paliperidone was transferred into a 50 ml volumetric flask containing 20 ml of mixed hydrotropic solution of 20% sodium benzoate and 20% Niacinamide. Shake vigorously for about 15 minutes to solubilize the drug, and the volume was adjusted to 50 ml mark with distilled water and then filtered through whatman filter paper no# 41. The filtrate was diluted appropriately with distilled water and was analysed on UV spectrophotometer at 286nm against corresponding reagent blank. Drug content of tablet formulation were calculated using calibration curve and the values are reported in Table 3.

METHOD VALIDATION

The developed method for quantitative estimation of Paliperidone was validated as per ICH guidelines in order to determine the linearity, sensitivity, precision, robustness and accuracy. (ICH Q2A.1994[10])To evaluate the validity and reproducibility of the method, known amount of pure drug was added to the pre-analyzed sample of tablet powder and the mixture was analyzed for the drug content using the proposed method. For this recovery study the tablet powder equivalent to 50mg each was taken in two 50ml volumetric flask and 10 mg of pure drug (spiked drug) was transferred to each flask and 20ml of hydrotropic blend was added and the flasks were shaken for about 10 minutes. Then the volume was made up to the mark with distilled water and filtered through whatman filter paper No#41. The solution was diluted appropriately with distilled water and analysed for drug content against corresponding reagent blank. The percentage recovery was found to be within range. (Table 4)

REPEATABILITY

Repeatability expresses the precision under the same operating conditions over short interval of time. The precision (of an analytical procedure) is usually expressed as the standard deviation of a series of measurement. The reproducibility of the method was studied using three different concentrations of Paliperidone (10, 20 and 30µg/ml) which were prepared from stock solution. The absorbance was measured at 286nm against corresponding reagent blank for three times and their mean values were calculated and data is given in table 5.

The intra-day and inter-day precision studies of Paliperidone were carried out by estimating the responses three times on the same day and on three different days (1st, 2nd &5th day) for different concentration of Paliperidone (10, 20 & 30µg/ml) and the results were reported in terms of relative standard deviation which is presented in table 6 and table 7.

Table 4: Data of Recovery Studies

No	Brand name	Drug added (spiked)mg	Amt found(mg)	Recovery estimated(mean ± s.d) n=6
1	Palido OD	10mg	15.9571	99.73±0.0231
2	Palivega	10mg	15.8093	98.81±0.0318

Table 5: Data for repeatability

No	Concentration (µg/ml)	Absorbance at 286nm	Mean value	Std deviation	Std error	Co-eff of variation
1	10	0.19692 0.19693 0.19691	0.19692	0.000009	0.000005	0.0028
2	20	0.39935 0.39936 0.39934	0.39935	0.00001	0.000005	0.0025
3	30	0.59158 0.59156 0.59160	0.59158	0.00002	0.00001	0.0033

Table 6: Intra-day precision

SI No	Concentration(µg/ml)	Absorbanceat 286nm			RSD%
		0hr	1.5hr	3hr	
1	10	0.19697	0.19692	0.19688	0.02289
2	20	0.39934	0.39930	0.39936	0.0076
3	30	0.59160	0.59158	0.59164	0.00516

Table 7: Inter-day precision

Sl no	Concentration (µg/ml)	Absorbance at 286nm			RSD%
		1st	2nd	5th	
1	10	0.19692	0.19688	0.19683	0.02290
2	20	0.39936	0.39933	0.39929	0.00879
3	30	0.59164	0.59161	0.59156	0.00683

DETECTION LIMIT (LOD)

The detection limit 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. The LOD of Paliperidone by the proposed method was found to be 0.6079 µg/ml.

QUANTITATION LIMIT (LOQ)

The quantitation limit of an individual analytical procedure is the lowest concentration of analyte in a sample, which can be quantitatively determined with a suitable level of precision & accuracy. The LOQ of Paliperidone by the proposed method was found to be 2.0265 µg/ml.

LINEARITY

The linearity of an analytical procedure is its ability to obtain test results which are proportional to the concentration of analyte in the sample. The calibration curve of Paliperidone was linear over the range 10-50 µg/ml.

RESULT & DISCUSSION

Normally quantitative estimation of poorly water soluble drugs involves the use of organic solvents. In the present investigation mixed hydrotropic solubilisation method was employed to enhance the aqueous solubility of poorly water soluble drugs like Paliperidone in bulk and tablet dosage forms. The solubility studies indicated that enhancement in aqueous solubility of Paliperidone in mixed hydrotropic solution containing 20% Sodium benzoate and20% Niacinamide solution was more than 87 folds as compared to their solubility in distilled water. Therefore this solution was employed to extract Paliperidone from the fine powder of tablet formulation.After solubilizing the Paliperidone in selected hydrotropic blend, it was scanned in spectrum mode, and the wave length for the estimation was found to be 286 nm. It is evident that there is good agreement between the amounts estimated and those claimed by the manufactures. The mean percentage label claims 99.48±0.292 and 98.01±0.326 for Palido OD and Palivega respectively (Table 3) are very close to 100 with low values of standard deviation and standard error, which confirms the accuracy of the proposed method. Accuracy, reproducibility and precision of the proposed method were further confirmed by the mean percentage recovery values (98.81±0.0318 to 99.73±0.0231) which were closer to 100 with low values of standard deviation (table 4). The developed method was found to be linear in the range of 10-50µg/ml. The linear regression of absorbance on concentration gave the equation Y= 0.019 x + 0.008 with a correlation coefficient r^2 of 0.9990 (figure 4).

CONCLUSION

The developed method is new, economic, simple, precise, environment friendly, accurate and reproducible. Hence it can be employed for routine analysis for the estimation of Paliperidone from marketed formulations. So it may be concluded that mixed hydrotropic solubilization method can be successfully employed in analytical estimation of water insoluble drugs.

ACKNOWLEDGEMENT

The authors thank Unichem Laboratories Ltd, Goa for the gift sample of Paliperidone andState Board of Medical Research(A2-SBMR/15790) for providing fund.Also greatful to College of Pharmaceutical Sciences Govt Medical College, Trivandrum for providing the facilities for the research work.

REFERENCES

1. R.S.Satoskar, N.N.Rege. Pharmacology and Pharmacotherapeutics. 23rd edition.Popular Prakashan. Mumbai. 2013.P.202
2. Deepak Ghogare, Sheetal Patil. Hydrotropic solubilisation: Tool for eco-friendly analysis. International Journal of Pharmacy and Pharmaceutical Research 2018: 11(3): 300-322
3. R.KMaheshwari. Solid as Solvent-Novel spectro photometric analysis of Norfloxacin tablets using phenol as solvent. International journal of current pharmaceutical Research.2014:6(4):76-78
4. R.K Maheshwari, Ravi Shanker Shukla. Novel method for spectrophotometric analysis of Hydrochlorthiazide tablets using Niacinamide as hydrotropic solubilizing agent. Asian Journal of Pharmaceutics. 2008: 1(2)A:68-69.
5. Snehal.B.Ghanwat,Rajendra.B.Patil. Stability indicating Analytical method development and validation for estimation of Paliperidone in bulk and its pharmaceutical dosage form. World Journal of Pharmacy and Pharmaceutical Sciences. 2017:6 (1):1382-1394
6. Bhushan M Firake,Harsha.P.Bhutada. Four UV Spectrophotometric methods for estimation of Paliperidone in bulk and their Pharmaceutical dosage form. Analytical Chemistry An Indian Journal. 2016:16(7): 277-287
7. Atul P Sherje,Vaishali Londhe.Stability indicating HPLC Method for determination of Paliperidone in bulk and pharmaceutical dosage form. International Journal of Pharm Tec Research. 2015:8(8):157-163
8. K.Nageswara Rao, Ganapathi.Development and validation of new HPLC Method for the estimation of Paliperidone in pharmaceutical dosage forms. Rasayan.J. Chem. 2013:6(1):34-38
9. K.Umamaheswar, G. Ramu. A reverse phase HPLC method development and validation for the determination of Paliperidone in pure and Dosage forms.Chemical Science Transactions.2013:2(1):41-46
10. ICH. Q2A Validation of analytical procedure- Guidelines, Methodology, International Conference on Harmonization. Steering Committee, Geneva : 1994:6-13