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Four UV spectrophotometric methods for estimation of paliperidone in bulk and their pharmaceutical dosage form

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ABSTRACT

A simple, precise and economical methods of UV Spectrophotometry for the estimation of Paliperidone (PPD) in bulk and its formulation are proposed. PPD was estimated at 238.2nm, 236.8nm, 232nm, 232nm in ethanol, ethanol and distilled water, diethyl ether, diethyl ether and distilled water, respectively. The precision expressed as relative standard deviation, which was within 2.0 % for the above four methods. These shows linearity over the concentration range of 0.2-1µg/ml, 5-25µg/ml, 2-10µg/ml, 10-100µg/ml with regression equation 0.018x + 0.004 (r^2 = 0.999), 0.179x + 0.017 (r^2 = 0.999), 0.180 + 0.042 (r^2 = 0.998), 0.100x - 0.077 (r^2 = 0.999). The proposed methods can be successfully applied for the determination of PPD in dosage forms.

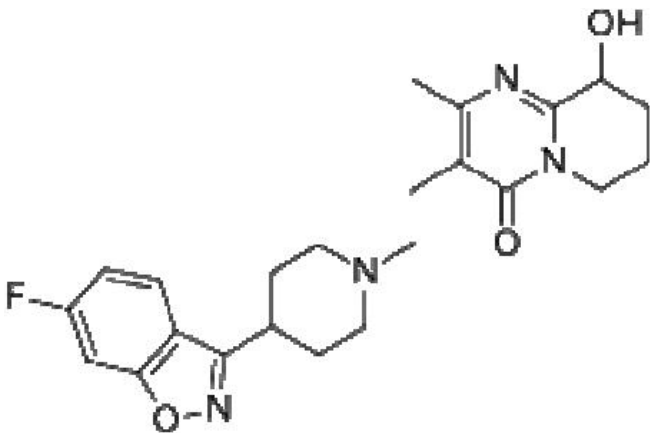
KEYWORDS

Paliperidone;
UV spectrophotometry.

INTRODUCTION

Paliperidone (PPD), the primary active metabolite of the older antipsychotic risperidone (9-hydroxy-risperidone), has been approved by the FDA for the treatment of schizophrenia since 2006. PPD is a centrally active dopamine D_2 & serotinergic 5-HT_2A antagonist. It is also active as an M antagonist at α_1 and α_2 adrenergic receptors and H_1-histaminergic receptors. Chemically it is (RS)-3-[2-[4-(6-fluorobenzo[d]isoxazol-3-yl)-1-piperidyl]ethyl]-7-hydroxy-4-methyl-1,5-diazabicyclo [4.4.0] deca-3, 5-dien-2-one. PPD has one chiral centre but as the pharmacological profile of the racemate & the two enantiomers are similar with respect to in vitro binding assays, in vitro receptors occupancy studies and in vivo functional interaction studies, hence, it is marketed in racemic mixture[1-5].

Literature survey reveals that few UV Spectrophotometric methods were reported for the



estimation of PPD using variety of solvents[6-15]. However, there is a need to develop a simple economic method that could be extended for estimation of PPD in small laboratories, industries.

EXPERIMENTAL

Materials

Bulk drugs and various available marketed formulations of the PPD (PPD) will be made use.

Equipments

Shimadzu 1800 UV Spectrophotometer with 1 cm matched quartz cell was used.

Solvents

Depending upon the solubility of the PPD, the AR grade selected solvents are as follows:

Ethanol,
Ethanol and Distilled Water,
Diethyl ether,
Diethyl ether and Distilled Water.

Solubility

Solubility of PPD was observed using number of solvents. It was found that PPD is soluble in chloroform, dichloromethane, ethanol, methanol and diethyl ether.

Standard drug solution

Method A: (solvent: ethanol)

Accurately weighed 10mg of PPD (bulk drug) was dissolved in 10ml of ethanol to obtain a concentration of 1000µg/ml (Stock Solution).

From the above stock solution, 1ml was pipetted out into10ml calibrated volumetric flask and volume was made up to the mark with ethanol to obtain a concentration of 100µg/ml.

From the above solution, again 1ml was pipetted out into 10ml calibrated volumetric flask and volume was made up to the mark with ethanol to obtain a final concentration of 10µg/ml (Working standard solution).

Method B: (Solvent system: ethanol + distilled water)

Accurately weighed 10mg of PPD (bulk drug) was dissolved in 10ml of ethanol to obtain a concentration of 1000µg/ml.

From the above stock solution, 1ml was pipetted out into10ml calibrated volumetric flask and volume was made up to the mark with distilled water to obtain a final concentration of 100µg/ml (Working standard solution).

Method C: (solvent: diethyl ether)

Accurately weighed 10mg of PPD (bulk drug) was dissolved in 10ml of diethyl ether to obtain a concentration of 1000µg/ml (Stock solution).

From the above stock solution, 1ml was pipetted

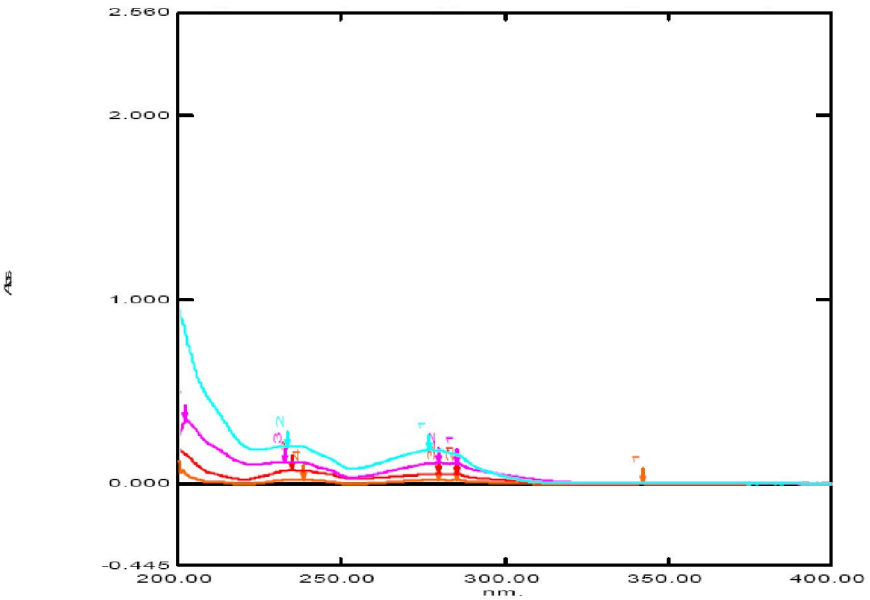


Figure 1 : Absorption spectrum (Overlay) of PPD using ethanol (method A)

TABLE 1 : Absorbance values of PPD using ethanol (method A)

Concentrations (µg/ml)	Absorbance
0.2	0.024
0.4	0.042
0.6	0.059
0.8	0.080
1.0	0.098

out into10ml calibrated volumetric flask and volume was made up to the mark with diethyl ether to obtain a final concentration of 100µg/ml (Working standard solution).

Method D: (Solvent system: diethyl ether + distilled water)

Accurately weighed 10mg of PPD (bulk drug) was dissolved in 10ml of diethyl ether to obtain a final concentration and further it is diluted with distilled water.

Preparation of calibration curve: Method A

Fresh aliquots from working standard solution (10µg/ml) of Method A, ranging from 0.2 to 1.0ml (1ml = 10µg) were transferred into a series of 10ml calibrated volumetric flasks and volumes were made up to the mark by ethanol to get final concentrations of 0.2 to 1µg/ml. The absorbance values of all the solutions were measured at 238.8nm against ethanol as a blank. Calibration curve was prepared by plotting absorbance versus concentration of drug.

TABLE 2 : Optical characteristics and precision (for method A)

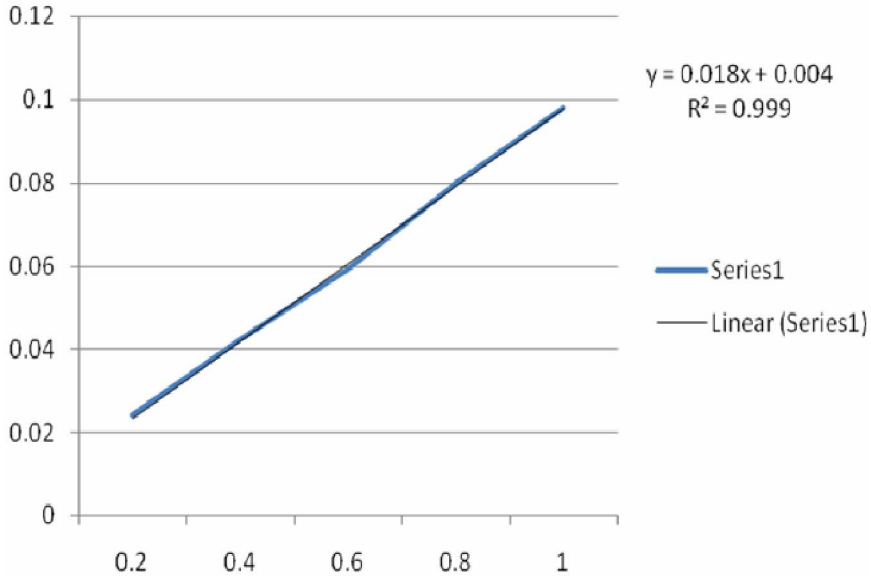
Parameters	UV Method
λmax	238.2nm
Beer's law limits(µg/ml)	0.2 to 1.0
Limit of Detection(µg/ml)	0.12
Limit of Quantification(µg/ml)	0.41
Regression equation(y*)	
Slope(m)	0.018
Intercept(c)	0.004
Correlation coefficient	0.9994
%RSD	1.542

Preparation of calibration curve: method B

Fresh aliquots from working standard solution (100µg/ml) of Method B, ranging from 0.5 to 2.5ml (1ml = 100µg) were transferred into a series of 10ml calibrated volumetric flasks and volumes were made up to the mark by distilled water to provide final concentrations of 5 to 25µg/ml. The absorbances of the solutions were measured at 236.8nm against distilled water as a blank. Calibration curve was prepared by plotting absorbance versus concentration of drug.

Preparation of calibration curve: method C

Fresh aliquots from working standard solution (10µg/ml) of Method C, ranging from 2 to 10ml were



y* = mx+c, where m=slope & c= intercept.

Figure 2 : Calibration curve of PPD using ethanol (method A)

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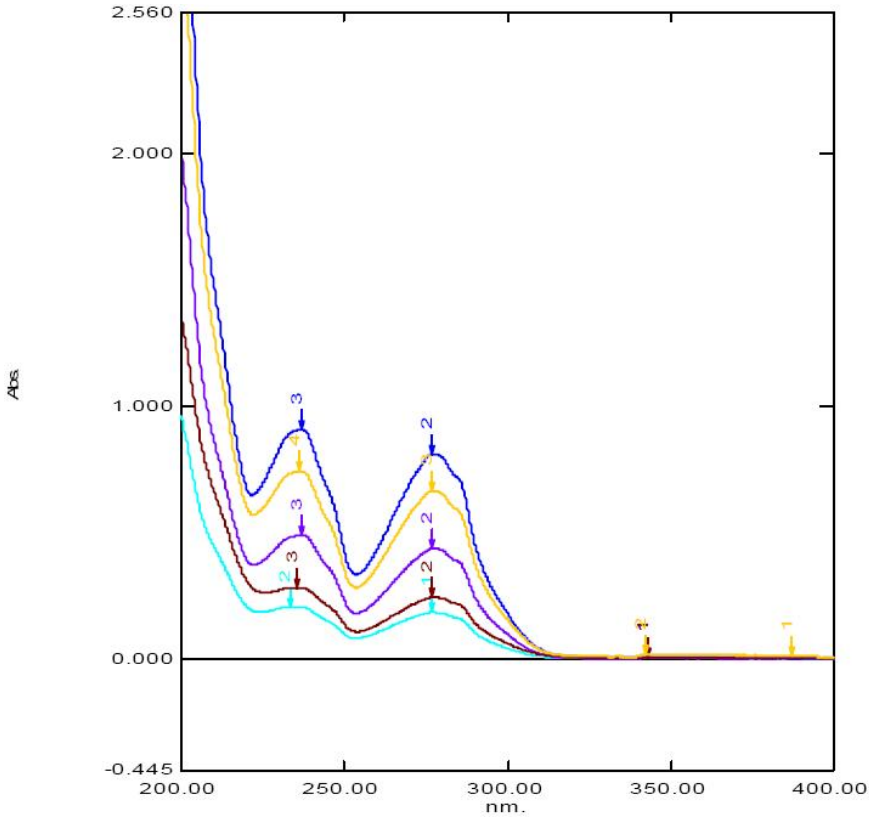

Figure 3 : Absorption spectrum (overlay) of PPD using ethanol + distilled water (method B)

TABLE 3 : Absorbance values of PPD using ethanol + distilled water (method B)

Concentrations (µg/ml)	Absorbance
5	0.203
10	0.366
15	0.552
20	0.747
25	0.906

transferred into a series of 10ml calibrated volumetric flasks and volumes were made up to the mark by diethyl ether to get the final concentrations of 2 to 10µg/ml. The absorbance values of the solutions were measured at 232nm against diethyl ether as a blank. Calibration curve was prepared by plotting absorbance versus concentration of drug.

Preparation of calibration curve: method D

Fresh aliquots from working standard solution (100µg/ml) of Method D, ranging from 1 to 10ml were transferred into a series of 10ml calibrated volumetric flasks and volumes were made up to the mark by distilled water to provide final concentrations of 10 to 100µg/ml. The absorbance values of the solutions were measured at 232nm against water as a blank. Calibration curve was prepared by plotting absorbance versus concentration of drug.

Assay procedure for pharmaceutical tablets (Method A):

For the analysis of PPD Extended Release, a brand of commercially available tablets was purchased. The sample of tablet claimed to contain 6mg of active drug. Twenty tablets were weighed and grounded into fine powder. An accurately weighed portion of the powder equivalent to 100mg of PPD was transferred into a 100ml volumetric flask containing small quantity of ethanol and solution was shaken thoroughly for about 10 to 15 minutes. The final volume (100ml) was made with ethanol to obtain a solution of 1000µg/ml (Stock solution).

From the stock solution, 10ml of the solution was pipetted out into a 100ml calibrated volumetric flask and volume was made up to the mark with ethanol to obtain concentration of 100µg/ml.

From this solution, 10ml was pipetted out into a 100ml calibrated volumetric flask and volume was

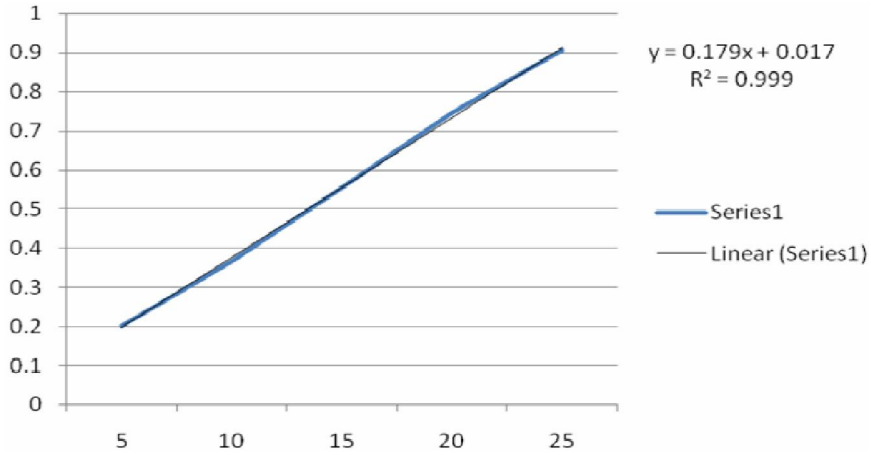

Figure 4 : Calibration Curve of PPD using ethanol + distilled water (method B)

TABLE 4: Optical characteristics and precision (for method B)

Parameters	UV Method
λmax	236.8 nm
Beer's law limits(µg/ml)	5-25
Limit of Detection(µg/ml)	2.39
Limit of Quantification(µg/ml)	7.90
Regression equation(y*)	
Slope(m)	0.179
Intercept(c)	0.017
Correlation coefficient	0.9994
%RSD	1.9500

made up to the mark with ethanol to obtain a concentration of 10µg/ml. From this solution, 0.6ml of the solution was pipetted out into a 10ml calibrated volumetric flask and volume was made up to the mark with ethanol to obtain a final concentration of 0.6µg/ml (Working solution) and was analyzed at the selective analytical wavelength of 238.2nm.

Assay procedure for pharmaceutical tablets (method B):

Twenty tablets were weighed and grounded into fine powder. An accurately weighed portion of the powder equivalent to 100mg of PPD was transferred into a 100ml volumetric flask containing small quantity of ethanol and solution was shaken thoroughly for about 10 to 15 min. The final volume (100ml) was made with ethanol to obtain a solution of 1000µg/ml (Stock solution).

From the stock solution 10ml of the solution was pipetted of into 100ml calibrated volumetric flask

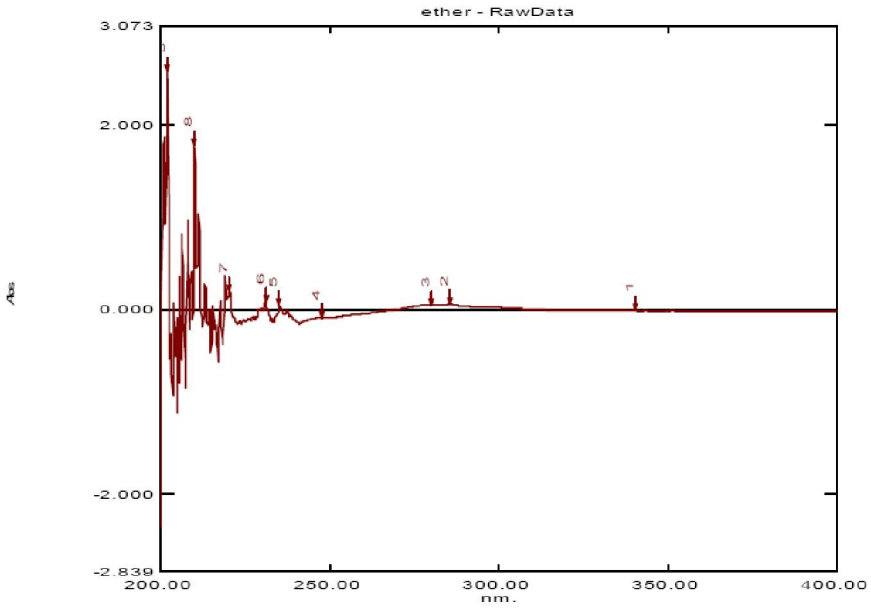

Figure 5 : Absorption spectrum of PPD using diethyl ether (method C)

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TABLE 5 : Absorbance values of PPD using diethyl ether (method C)

Concentrations (µg/ml)	Absorbance
2	0.212
4	0.415
6	0.585
8	0.775
10	0.935

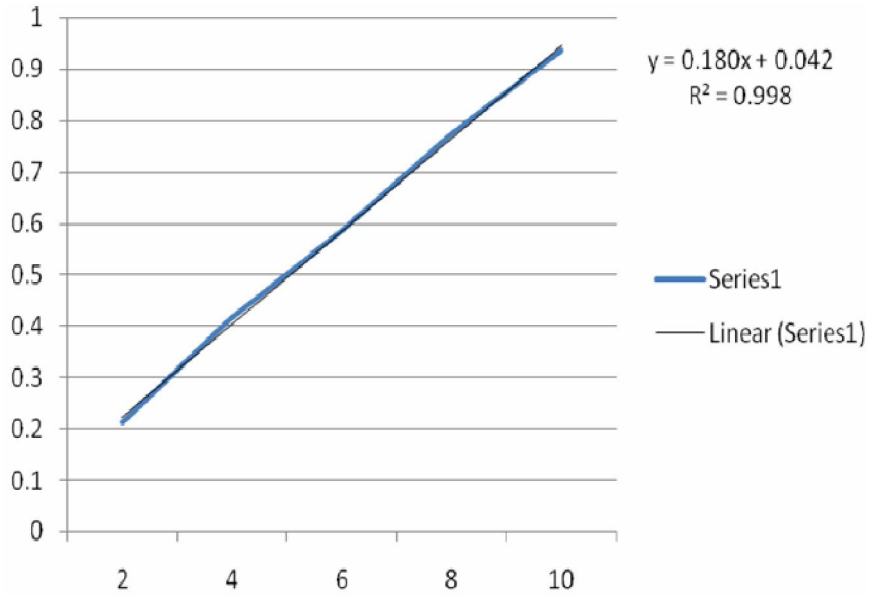

Figure 6 : Calibration curve of PPD using diethyl ether (method C)

TABLE 6 : Optical characteristics and precision (for method C)

Parameters	UV Method
λmax	232.0 nm
Beer's law limits (µg/ml)	2-10
Limit of Detection(µg/ml)	0.51
Limit of Quantification(µg/ml)	1.68
Regression equation(y*)	
Slope(m)	0.180
Intercept(c)	0.042
Correlation coefficient	0.9989
%RSD	1.621

and volume was made up to the mark with distilled water to obtain concentration of 100µg/ml. From this solution, 2ml of the solution was pipetted out into a 10ml calibrated volumetric flask and volume was made up to mark with distilled water to obtain a final concentration of 20µg/ml (Working solution), and was analyzed at the selective analytical wavelength of 236.8nm.

Assay procedure for pharmaceutical tablets (method C):

Twenty tablets were weighed and grounded into fine powder. An accurately weighed portion of the powder equivalent to 100mg of PPD was transferred into a 100ml volumetric flask containing small quantity of diethyl ether and solution was shaken thoroughly for about 10 to 15 min. The final volume (100ml) was made with diethyl ether to obtain a solution of 1000µg/ml (Stock solution). From the stock solution, 10ml of the solution was pipetted of into a 100ml calibrated volumetric flask and volume was made up to the mark with diethyl ether to obtain a concentration of 100µg/ml. From this solution, 10ml of the solution was pipetted out into a 100ml calibrated volumetric flask and volume was made up to the mark with diethyl ether to obtain a concentration of 10µg/ml. From this solution, 4ml of the solution was pipetted out into a 10ml calibrated volumetric flask and volume was made up to mark with diethyl ether to obtain a final concentration of 4µg/ml (Working solution), and was analyzed at the selective analytical wavelength of 232nm.

Assay procedure for pharmaceutical tablets (method D):

Twenty tablets were weighed and grounded into fine powder. An accurately weighed portion of the powder equivalent to 100mg of PPD was transferred

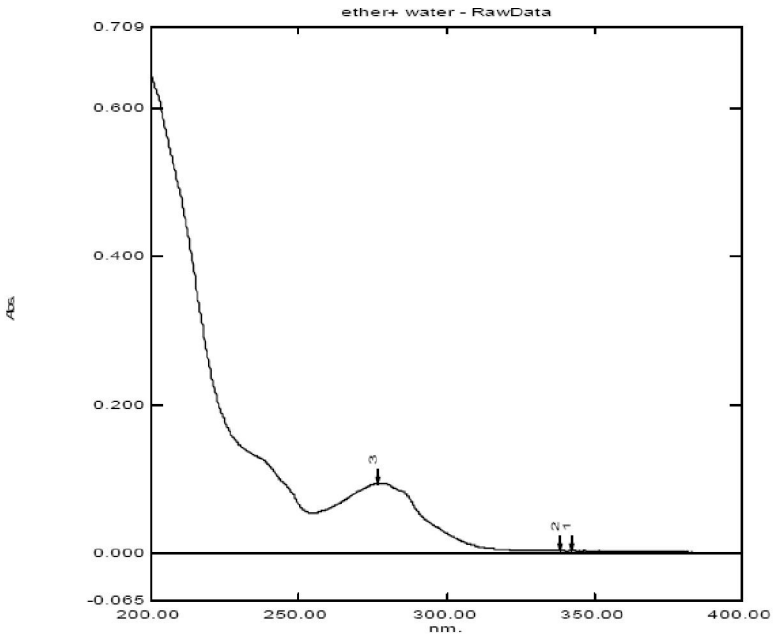

Figure 7 : Absorption spectrum of PPD using diethyl ether + distilled water (method D)

TABLE 7 : Absorbance values of PPD using diethyl ether + distilled water (Method D)

Concentrations (µg/ml)	Absorbance
10	0.025
20	0.108
30	0.225
40	0.331
50	0.420
60	0.532
70	0.640
80	0.724
90	0.842
100	0.963

into a 100ml volumetric flask containing small quantity of diethyl ether and solution was shaken thoroughly for about 10 to 15 min. The final volume (100ml) was made with diethyl ether to obtain a solution of 1000µg/ml (Stock solution). From the stock solution, 10ml of the solution was pipetted out into a 100ml calibrated volumetric flask and volume was made up to the mark with distilled water to obtain concentration of 100µg/ml. From this solution, 5ml was pipetted out into a 10ml calibrated volumetric flask and volume was made up to the mark with distilled water to obtain a final concentration of 50µg/ml (Working solution), and was analyzed at the selective analytical wavelength of 232nm.

TABLE 8 : Optical characteristics and precision (for method D)

Parameters	UV Method
λmax	232.0 nm
Beer's law limits (µg/ml)	10-100
Limit of Detection (µg/ml)	2.83
Limit of Quantification (µg/ml)	9.35
Regression equation(y*)	
Slope(m)	0.100
Intercept(c)	-0.077
Correlation coefficient	0.9994
%RSD	1.984

Formula

The amount of PPD the sample and its % purity were computed from

Amount of drug(mg)= (A_T / A_S) × Conc. of standard × dilution factor × Average weight

% Purity= (Amount of drug in mg × 100) / Label Claim

RESULTS AND DISCUSSION

Results

The assays showed 99.16%, 99.33%, 97.00%, 99.50% purity of the pharmaceutical dosage form.

Recovery studies[16]

Recovery studies were carried out by addition

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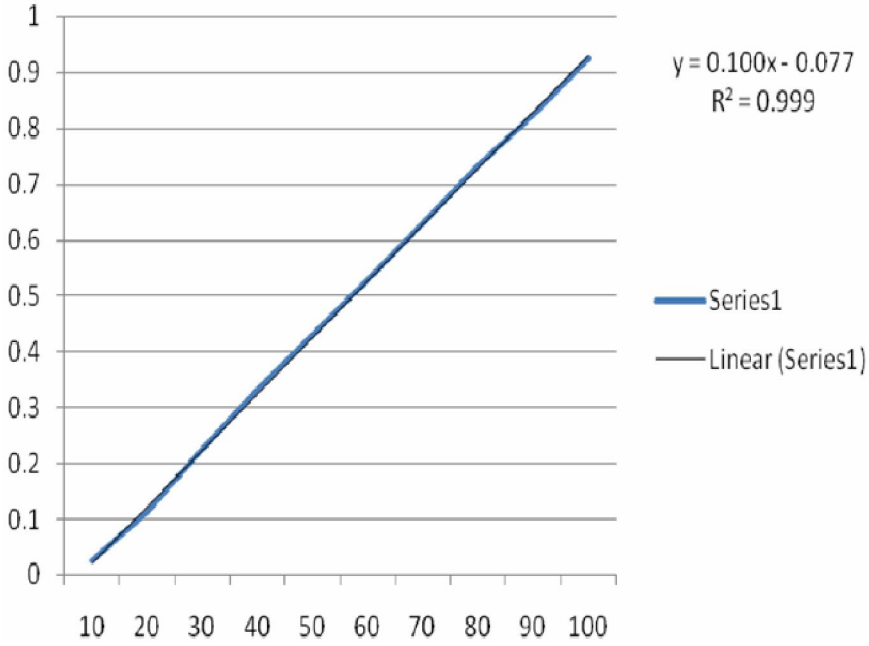

Figure 8 : Calibration curve of PPD using diethyl ether + distilled water (method D)

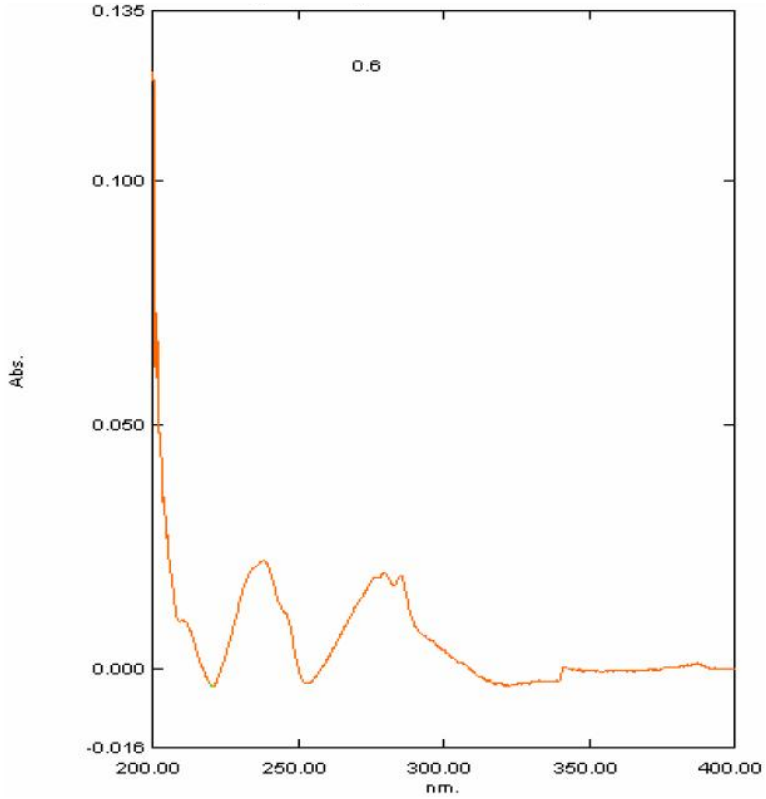

Figure 9 : Absorption spectrum of PPD in its pharmaceutical dosage form (method A)

of standard drug solution to preanalyzed sample. Results of recovery studies were found to be satisfactory and are presented in TABLE 10.

DISCUSSION

PPD was estimated at 238.2nm, 236.8nm, 232nm, 232nm in ethanol, ethanol and distilled water, diethyl ether, diethyl ether and distilled water, respectively (Figure 1, 3, 5, and 7). The optical characteristics are summarized in TABLE 2, 4, 6, 8.

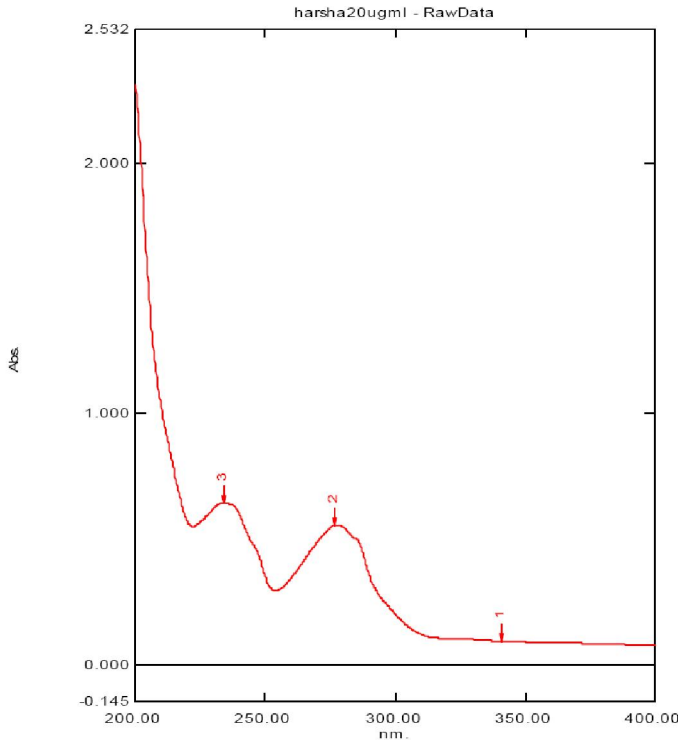

Figure 10 : Absorption spectrum of PPD in its pharmaceutical dosage form (method B)

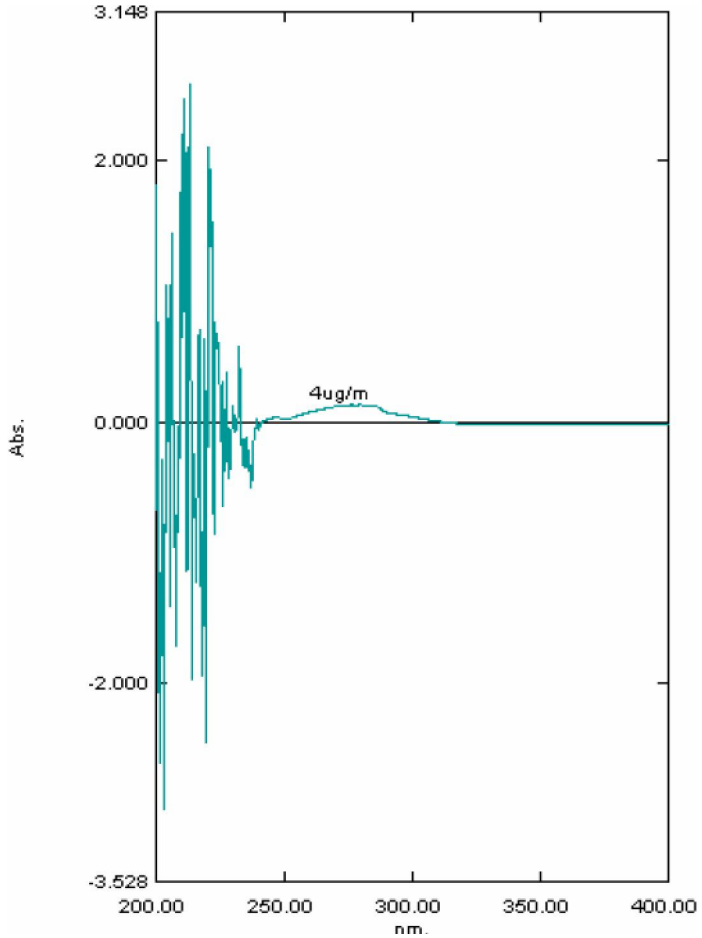

Figure 11 : Absorption spectrum of PPD in its pharmaceutical dosage form (method C)

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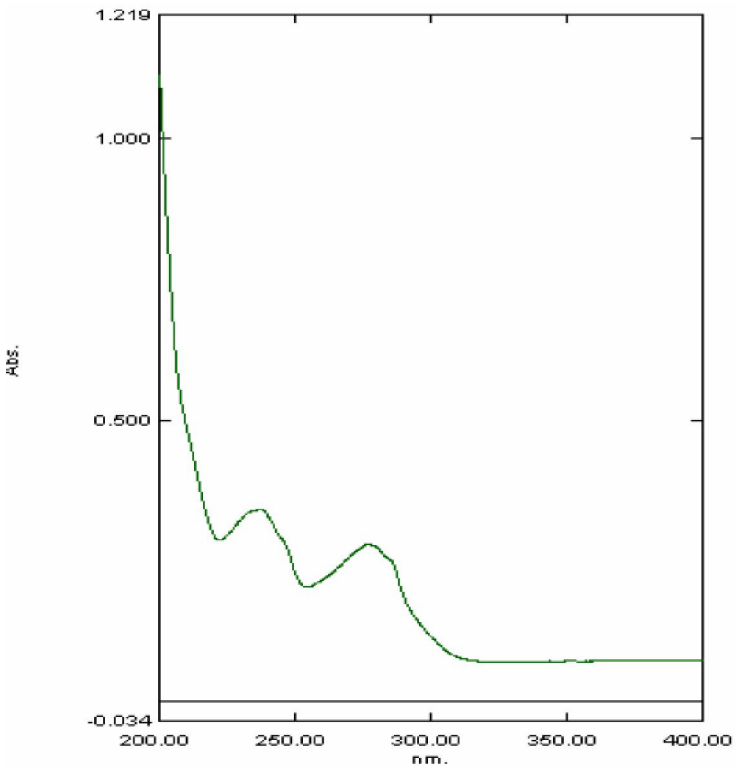

Figure 12 : Absorption spectrum of PPD in its pharmaceutical dosage form (method D)

TABLE 9 : Evaluation of PPD in pharmaceutical dosage form (tablet)

Methods adopted	Sample	Labelled amount (mg)	Amount of drug found by the proposed method (mg)	% Recovery of the proposed method
Method A	T_1	6	5.95	99.16
Method B		6	5.96	99.33
Method C		6	5.82	97.00
Method D		6	5.97	99.50

TABLE 10 : Result of recovery studies

Methods	Concentration of added drug to final solution (µg/ml)	% Recovery	Mean
Method A	2	101.86	100.95
	4	99.79	
	6	101.20	
Method B	2	102.27	101.44
	4	101.24	
	6	100.82	
Method C	2	98.80	97.37
	4	95.20	
	6	98.12	
Method D	2	101.19	99.86
	4	100.20	
	6	98.20	

The results showed that the four methods has reasonable precision with low % R.S.D. Assay showed 99.16%, 99.33%, 97.00%, 99.50% purity of the pharmaceutical dosage form (TABLE 9). The linearity of all the methods was established from the regression line equation. The results showed a

linear relationship between concentration and absorbance for the range of 0.2-1.0µg/ml, 5-25µg/ml, 2-10µg/ml, and 10-100µg/ml. The results of recovery studies were found to be satisfactory (TABLE 10).

CONCLUSION

The proposed methods were found to be economic, accurate, precise, linear, less time consuming with sensitivity. Thus it can be extended for routine analysis of PPD in pharmaceutical industries, hospitals and research laboratories.

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