Innovare Academic Sciences

International Journal of Pharmacy and Pharmaceutical Sciences

ISSN- 0975-1491 Vol 7, Issue 7, 2015

Short Communication

DEVELOPMENT AND VALIDATION OF UV SPECTROMETRIC METHOD FOR QUANTITATIVE DETERMINATION OF ULIPRISTAL ACETATE

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Received: 08 Apr 2015 Revised and Accepted: 11 May 2015

ABSTRACT

Objective: To develop and validate UV spectrometric method for quantitative determination of ulipristal acetate.

Methods: The solvent selected was methanol and detection was carried out at 302 nm.

Results: Linearity of the proposed method was found to be between 5–20 µg/ml. LOD and LOQ were found to be 0.0062 µg/ml and 0.0187 µg/ml, respectively. The % recovery of the proposed method was found to be 98.83 %-100.32 %. The method was found to be precise as the values of % RSD obtained for both intraday and interday, precision studies were found to be<2.0 %. The method was robust and can be useful for routine analysis of formulations containing ulipristal acetate.

Conclusion: The developed method was found to be simple, sensitive, linear, accurate, precise and robust. The developed and validated method can be used for quantitative determination of ulipristal acetate in bulk drugs and dosage form.

Keywords: Ulipristal acetate (UPA), UV spectrometry, Validation, Quantitation.

INTRODUCTION

Ulipristal acetate (UPA), chemically 19-norprogesterone [17 alpha-acetoxy-11-(4-N,N-dimethylaminophenyl)-19-norpregna-4,9-diene-3,20-dione](fig. 1), is a progesterone receptor modulator with contraceptive potential. It is white amorphous powder, sparingly soluble in water and freely soluble in methanol, acetonitrile and chloroform. UPA prevents progesterone from binding to the receptor, leading to blockage of gene transcription inhibiting synthesis of proteins necessary to begin and maintain pregnancy [1]. It also acts by inhibiting the ovulation. The drug has also shown potential in the treatment of uterine fibroids [2, 3]. Ulipristal acetate is available in tablet dosage form (ella One 30 mg) [4, 5].

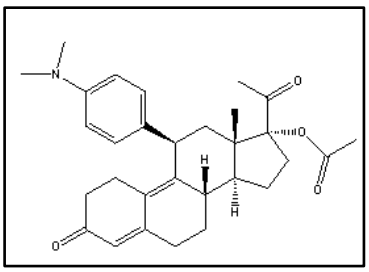

Fig. 1: Structure of ulipristal acetate

As per literature review, no UV spectrometric method is reported for quantitative estimation of ulipristal acetate. Hence, the aim of the present study was to develop and validate a fast, simple, selective, sensitive and inexpensive UV spectrometric method for the quantitative estimation of ulipristal acetate in tablet dosage form.

A double beam Agilent cary 60 UV-visible spectrophotometer and single beam Thermo Electron Corporation Helious α UV-visible spectrophotometer were used. Standard of ulipristal acetate was obtained as gift sample from authentic source. Methanol AR used as solvent was procured from Rankem (RFCL), Gujarat, India.

Standard stock solution containing ulipristal acetate was prepared by dissolving 10 mg of drug in 50 ml of methanol, it was then sonicated for 10 minutes and the final volume of the solution was made up to 100 ml with methanol to get stock solution containing 100 µg/ml of ulipristal acetate. For test solution, twenty tablets of ulipristal acetate (each tablet containing 30 mg of ulipristal acetate) were weighed; average weight was calculated and triturated. Accurately weighed tablet powder containing 25 mg of ulipristal acetate was transferred to a 250 ml of volumetric flask. About 50 ml of methanol was added to the flask and sonicated for 15 min. The volume of the solution was made up to the mark to get solution containing 100µg/ml of ulipristal acetate. The resulting solution was then filtered through a Whatman filter paper followed by syringe filter (Sartorius stedim biotech, Minisart).

Methanol was selected as solvent as the drug was found to be freely soluble in it. All the measurements were carried out at 302 nm which corresponds to absorbance maxima of the drug (fig. 2 & 3).

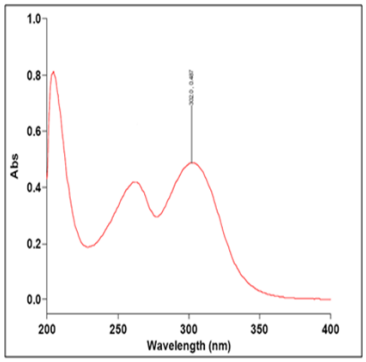

Fig. 2: UV spectrum of standard solution (10 µg/ml)

The developed method was validated as per ICH guidelines for various parameters such as specificity, linearity and range, LOD & LOQ, accuracy, precision and robustness [6].

The specificity of an analytical method is its ability to assess unequivocally the analyte in the presence of other components. Specificity was evaluated by comparison of spectra of 10 µg/ml of standard and test solutions containing UPA. The method was found to be specific as no interference was observed from the components present in the tablets.

The linearity of proposed method was evaluated by analyzing different concentration of the standard solutions of UPA in the range of 5–20 µg/ml. Absorbance of each solution was measured in triplicate at 302 nm using methanol as blank. A plot of average absorbance vs concentration was plotted and regression coefficient (R^2) was found to be 0.9991(fig. 4, table 1).

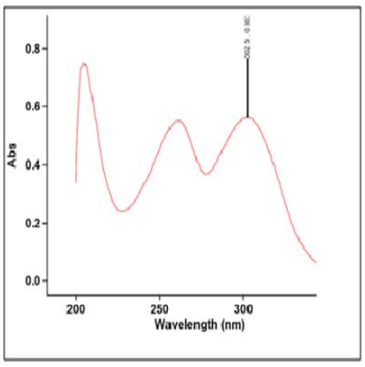

Fig. 3: UVspectrum of test solution (10 µg/ml)

Detection limit and quantitation limit represents sensitivity of the method. The LOD and LOQ of UPA were determined using standard deviation method. Calibration curve was prepared in the detection and quantitation range (1–6 µg/ml) and LOD and LOQ were determined using formula 3.3 σ/S and 10 σ/S, respectively, where S is the slope of the calibration curve and σ is the standard deviation of y–intercepts of calibration line. The LOD and LOQ of the proposed method were found to be 0.0062 µg/ml and 0.0187 µg/ml, respectively (table 1).

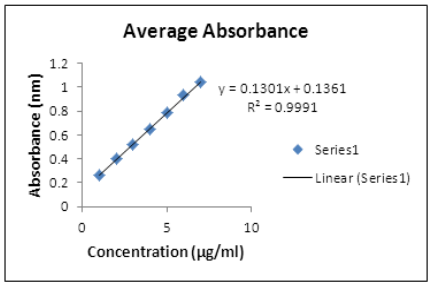

Fig. 4: Calibration curve of ulipristal acetate

Table 1: Results of quantitative determination of ulipristal acetate

S. No.	Parameters	Results*
1	Absorbance maximum (nm)	302
2	Linearity and Range (µg/ml)	5–20
3	Slope	0.1301
4	Intercept	0.1360
5	Correlation coefficient	0.9991
6	LOD (µg/ml)	0.0062
7	LOQ(µg/ml)	0.0187

*n = 3 (triplicate measurements)

To ascertain the accuracy of the proposed method, recovery studies were carried at three different concentration levels. Known amount of standard UPA solution (5µg/ml, 10 µg/ml, 15µg/ml) was added to pre analyzed test sample (2 µg/ml) and absorbance was recorded in triplicates.

Percent recovery for UPA at each level was calculated using formula: (Measured value/True value) x 100. Recovery at each level for the proposed method was found between 98.83 %-100.32 % with % RSD not more than 2.0 % (table 2) indicating the accuracy of the method.

Table 2: Results of accuracy studies of proposed method

Level	Amount added		% Recovery*±S. D.	% RSD*
	Standard (µg/ml)	Test(µg/ml)		
50 %	5	2	100.32±0.12	0.1218
100 %	10	2	98.83±0.06	0.0687
150 %	15	2	99.12±0.03	0.0374

*n = 3 (triplicate measurements)

The precision of the method was demonstrated by intraday and interday precision studies. In intraday precision studies, test samples were prepared at three concentration levels(5 µg/ml, 10 µg/ml, 15µg/ml) and absorbance were measured at different time intervals. While interday precision studies were carried out by analyzing sample solutions at three concentration levels for three different days. % RSD was determined for each concentration level. The values of % RSD obtained at each level of intraday and interday precision studies were less than 2 (table 3). Hence, the method was found to be precise.

Table 3: Results of precision studies of proposed method

Conc (µg/ml)	Intraday precision (% RSD)*		Interday precision (% RSD)*		
	Day 1	Day 1	Day 1	Day 2	Day 3
5	0.0000	0.0254	0.0756	0.0952	0.0266
10	0.0222	0.0129	0.0128	0.0129	0.0225
15	0.0538	0.0389	0.0306	0.0752	0.0085

*n = 3 (triplicate measurements)

The robustness of the proposed method was evaluated by varying method parameters such as different analysts (analyst 1, analyst 2), wavelengths (301 nm, 303 nm) and instruments (Agilent cary 60 UV-visible spectrophotometer, Thermo Electron Corporation Helious α UV-visible spectrophotometer). The robustness was assessed by analyzing standard solutions of 10 µg/ml (n = 6) and the sample solution of 2 µg/ml (n = 2) of UPA and % RSD was calculated. The low values of % RSD obtained after small deliberate changes of conditions used for the method indicate that the method was robust (table 4).

The in-house tablets containing 30 mg of UPA was prepared and analyzed. The content of UPA in tablets was found to be 102.20±0.00 table 5.

Table 4: Results of robustness studies of proposed method

Parameters		Absorbance±S. D.*	% RSD*	Content of UPA (mg)±S. D.* (mg)
Analyst	Analyst 1	0.5621±0.00	0.0145	29.66±0.00
	Analyst 2	0.5596±0.00	0.0246	29.66±0.00
Wavelength	301 nm	0.5602±0.00	0.0281	30.00±0.00
	303 nm	0.5701±0.00	0.0143	29.33±0.00
Instruments	Agilent cary 60	0.5622±0.00	0.0331	29.66±0.17
	Thermo Electron Corporation	0.5611±0.00	0.0776	29.66±0.00

*n = 6 (six measurements)

Table 5: Analysis of in-house tablets

Conc (µg/ml)	Absorbance	Label claim (mg)	Amount obtained*±S. D.	% Assay*±S. D.
10	0.5456	30	30.66±0.00	102.20±0.00
	0.5450			
	0.5451			

*n = 3 (triplicate measurements)

The proposed UV method is simple, sensitive, accurate, precise and robust. The proposed method is inexpensive and do not require any sophisticated apparatus in contrast to chromatographic methods. The method can be successfully used for routine quality control analysis of the formulation containing UPA.

CONFLICT OF INTERESTS

Declared None

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