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QUICK AND SIMPLE SPECTROPHOTOMETRIC METHOD FOR ESTIMATION OF RU486 IN TABLET DOSAGE FORM

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ABSTRACT

A new, simple and accurate Zero Order UV- Spectrophotometric method has been developed for quick determination of Mifepristone (RU486) in tablet formulation. Methanol was uesd as solvent. The method is based upon determination of RU486 at 303.8 nm. Beer's law obeyed the concentration range of 4 – 14 µg/ml. The % recovery was found in the range of 96.8 – 98 %. The % RSD value was found to be less than 0.66 %. Thus the proposed method was simple, economic, rapid, accurate and can be succesfully applied for determination of Mifepristone in tablet dosage form.

KEYWORDS: Mifepristone, RU486, Zero Order UV spectrophotometry.

INTRODUCTION

As a derivative of progestine Norethindrone, Mifepristone is a synthetic, steroidal antiprogesterone and antiglucocorticoid agent. It is used as a contraceptive, aborficiant agent to terminate pragnancy as a competitive inhibitor of progesterone, as a treatment for endometriosis (growth of uterus tissue outside the uterus) or fibroids (noncancerous tumors in the uterus) and progesterone sensitive tumors. So Mifepristone (MPT) is chemically, 11β-[p-(Dimethylamino) phenyl]-17β-hydroxy-17-(1-propynyl) estra-4, 9-dien-3-one. The empirical formula is $C_{29}H_{35}NO_2$, Mifepristone is pale yellow powder. It is very soluble in methanol, chloroform and acetone; and poorly soluble in water (0.00336 mg/ml). The structural formula is shown in fig (1).

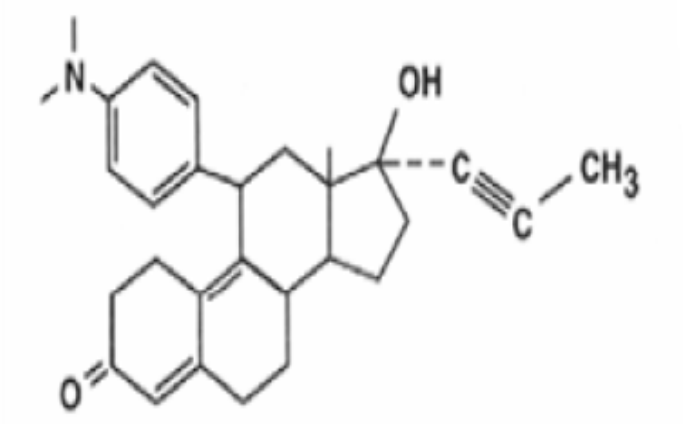

Figure 1: Structure of Mifepriston.

MATERIAL AND METHODS

Instruments

A shimadzu model 1700 (Japan) double beam UV/Visible spectrophotometer with spectral width of 2 nm, wavelenth accuracy of 0.5 nm and a pair of 10 mm matched quartz cell was used to measure absorbance of all the solutions. Spectra were automatically obtained by UV-probe 2.0 systemsoftware. A sartorious CP224S analytical balance (Gottingen, Germany), an ultrasonic bath (Frontline FS 4, Mumbai, India) was used in the study.

MATERIALS AND REAGENTS

Pure sample of MPT was provided as gift sample from Intas pharmaceuticals pvt ltd Ahmedabad. Tablet of label claim 200 mg mifepristone was procured from local market. Methanol AR Grade was received from S.D fine Chemicals Ltd, Mumbai, India. Whatman filter paper no.41 was used for filtration.

Selection of solvent

It was based on solubility and stability of drug in solvent system as well as extraction of drug from it formulation. MPT is insoluble in water but very soluble in methanol; hence methanol was selected as a solvent for its UV spectrophotometric determination.

Preparation of solution

Preparation of standard stock solution

A quantity of standard powder equivalent to 10 mg of MPT was transffered to a 100 ml volumetric flask. Methanol (50 ml) was added, sonicated for 30-35 min to dissove drug as perfectly as desirable. The solution was filtered through a Whatman filter paper No.41. The volume was fixed up to the mark with methanol.

Preparation of working standard solution

An aliquot of the standard stock solution concentation 100µg/ml (1 ml) was transferred in to a 10 ml volumetric flask and the volume was fixed upto mark with methanol to get final concentration of 10µg/ml.

Determination of wavelenth

The working standard dolution of MPT was scanned in UV range from 200-400 nm. The wavelenth maximawas found to be 259.2 nm and 303.8 nm (fig. 3). However, at 259.8 nm solution did not show better absorbance response and linearity. Hence 303.8 nm was choosen as the wavelenth for its estimation.

Zero Order Spectrophotometric method

It is the simple method for estimation of MPT in single drug formulation. In which, sample drug is dissolved into solvent and the wavelenth maxima has to be find out. By compairing it with standard solution concentration, the concentration of sample solution can be calculated.

Twenty tablets manufactured by INTAS (India) containing 200mg of MPT were taken, their average weight was determined and crushed to fine powder. A quantity of tablet powder equivalent to 10 mg of MPT was transferred to 100ml volumetric flask and dissolved in methanol and sonicated for 30 minutes. The volume was made up to 100 ml (1000µg/ml). The solution was filtered using Whatman paper No. 41. It was further diluted to get a solution containing 10µg/ml of MPT. This solution was analyzed at 303.8 nm and absorbance value obtained was substituted in equation for single point standardization to obtain the content of MPT. Results are shown in table -1.

$$\mathbf{C_{test} = A_{test} \times C_{standard} \div A_{standard}}$$

C_{test}: concentration in sample solution.

$C_{standard}$: concentration in standard solution.

A_{test} : absorbance of sample solution.

$A_{standard}$ -: absorbance of standard solution.

METHOD VALIDATION

The developed method was validated with respect to linearity, accuracy, intraday and interday precision, limit of detection (LOD) and limit of quantification (LOQ) and robustness in accordance with the ICH guideline.

Linearity

The calibration curve was constructed over a concentration range of 4-14 µg/ml (fig. 2). accurately measured working standard solutions of MPT (0.4, 0.6, 0.8, 1.0, 1.2 and 1.4 ml) were transferred to a series of 10 ml of volumetric flask and diluted to the mark with methanol. And absorbance was measured at 303.8 nm ((λmax of MPT). The calibration curve was assembled by constructing absorbances versus concentractions and the regression equations were calculated. Results are reported in table- 2.

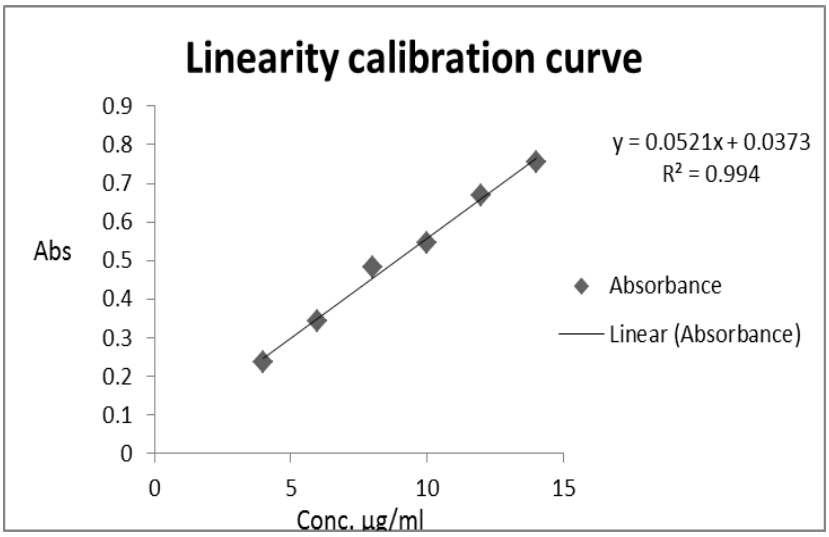

Figure 2: Linearity curve of Mifepristone.

Precision

The precision of an analytical procedure expresses the closeness of agreement (degree of scatter) between a series of measurements obtained from multiple sampling of the same sample under the prescribed conditions. Precision may be considered at three levels: repeatability, Intra day precision, Interday precision.

Repeatability

Repeatability of the method was determined by analyzing standard solution of MPT (5µg/ml) 6 times without changing the parameters of measurement. The results are reported in terms of relative standard deviation (RSD) in Table -2.

Intermediate precision

The intraday and interday precision of the proposed method was perfomed by analyzing the corresponding responses three times on the same day (intraday) and on three different days

(interday) over a period of one week for three different concentrations of standard solutions of MPT. Result was showed in Table-2.

Accuracy

Accuracy was checked by recovery study at 3 different concentration levels, i.e., a multilevel recovery study. The tablet samples were spiked with an extra 50, 100 and 150 % of standard MPT and the tablet formulation were analysed by proposed method. Results of the recovery study are shown in table 4 suggested that method was accurate for the estimation of MPT in tablet formulations. Result was showed in Table-3.

Limit of detection and limit of quantification

The limit of detection (LOD) and limit of quantification (LOD) were calculated using signal-to-noise (i.e. 3.3 for LOD and 10 for LOQ) ratio using following equations desinated:

LOD = 3.3 X σ/S

LOQ = 10 X σ/S

Where, σ = the standard deviation of the response,

S = slope of the calibration curve.

Ruggedness

Ruggedness of the method was determined by carrying out the analysis by different analyst and the absorbance of 5 µg/ml solution of MPT was noted. The result is shown in table-4.

RESULT AND DISCUSSION

An attempt has been made to develop a quick, economic, precise and accurate analytical method for estimation of MPT in tablet dosage form. The proposed methods are based on zero order spectophotometric absorption for the quick estimation of MPT in UV region using methanol as solvent. MPT obeyed linearity in the concentration range of 4-14µg/ml in the methanol at their respective λ-max with correlation coefficient (r^2 = 0.9993). The spectrum of MPT in methanol is shown in Figure 2.

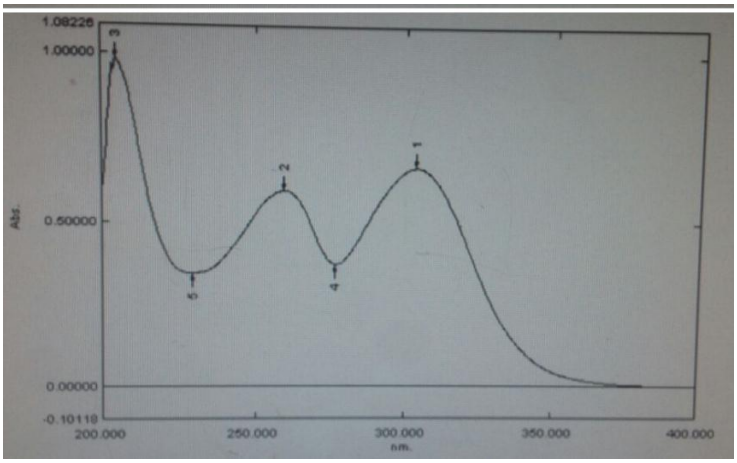

Figure 3: spectrum of MPT in methanol (10µg/ml).

Table 1: Estimation of MPT in Tablet Dosage Form.

MPT tablet dosage form	Labeled claim (mg/ml)	Amount found (mg/ml)	% Labeled Claim
	200 mg/ml	204	102 %

Table 2: Regression Data of MPT by Zero Order Spectophotometric Method.

Parameters		MPT(303.8 nm)
Beer's law limit (µg /ml)		4 – 14
Regression equation (y = mx + c)		y= 0.0521x + 0.0373
Slope		0.0521
Intercept		0.0373
Correlation coefficient (r^2)		0.9994
LOD (µg /ml)		0.2627
LOQ (µg /ml)		0.7961
Repeatability (% RSD, n =6)		0.9310
Precision (n=6) % RSD	Intraday	0.7017
	Interday	1.98

Table 3: Accuracy (% Recovery Study) Data for MPT.

Drug	Level	Amount taken (µg/ml)	Amount added (%)	% Recovery ± S.D. (n = 3)
MPT	I	5	50	97.25 ± 0.378
	II	5	100	98 ± 1.4
	III	5	150	96.8 ± 1.249

Table 4: Ruggedness of MPT.

Obaservation	Absorbance of MPT 5 µg/ml	% SD	%RSD
Analyst 1	0.34729	0.007046	1.98
Analyst 2	0.3562		
Analyst 3	0.3612		

CONCLUSION

The Zero Order UV Spectrophotometric method was developed for quick determination of MPT in tablet dosage form. Method was found to be simple, accurate, economic and quick as can be reflected from validation parameters data. Developed method was efficiently applied for determination of MPT in pharmaceutical formulation and therefor method can be extended for the regular QC analysis in tablet.

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REFERENCES

1. Hazara B.G., Pore V.S. Mifepristone (RU486), the recently developed sntiprogesterone drug and its analogues. Journal of Indian Institute and Science, 2001: 81: 287-98.
2. Tripathi KD, Essential of Medical Pharmacology, 7th edition, Hormones And Related Drugs, Jaypee Brothers, New Delhi, 2013; 319.
3. Methods of abortion,society for the Protection of Unborn Children, 3 Whitacre Mews, Stannary Street, London, SE11 4AB, United Kingdom.
4. Devadasu CH, Harika S, Mallikarjuna T, Adilakshmi G, Sreenath A. A Spectrophotometric Assay for the Simultaneous Analysis of Mifepristone and Misoprostol in Tablets Using Vierodt's and Absorbance Ratio Methods. Research Journal of Pharmacy and Technology., 2012; 5(1): 46-9.
5. Giri A, Saritha B, Reddy VG, Reddy ST. Quantitative Determination of Mifepristone in Pharmaceutical Samples By, Visible Spectrophotometric Method Using Ce (IV) As an Analytical Reagent, International Journal of Pharmaceutical Sciences and Drug Research., 2014; 6(3): 246- 9.
6. Giri A, Saritha B, Reddy VB, Reddy ST. A Simple, Visible Spectrophotometric Method for the assay of Mifepristone In Pharmaceutical Formulations Using Fe(iii) As An Analytical Reagent. International Journal of Innovative Pharmaceutical Sciences and Research., 2014; 2(5): 1006- 18.

7. Giri A, Saritha B, Reddy VB, Reddy ST. Validated Visible Spectrophotometric Method for The Estimation Of Mifepristone Using Cr (VI) As An Analytical Reagent. International Journal of Pharmacy and Therapeutics,. 2014; 5(4): 277- 82.
8. Guo Z, Wang S, Wei D, Zhai J. Development of a high-performance liquid chromatographic method for the determination of mifepristone in human plasma using norethisterone as an internal standard: application to pharmacokinetic study. Contraception,. 2007; 76: 228- 32.
9. Stith C, Hussain MD. Determination of mifepristone levels in wild canid serum using liquid chromatography. Journal of Chromatography B., 2003; 794: 9-15.
10. Geo Z, Chu C, Yin G, He M, Fu K, Wu J. An HPLC method for the determination of ng mifepristone in human plasma. Journal of Chromatography B., 2006; 832: 181– 4.
11. Guo Z, Wei D, Yin G, Wang S, Zhao S, Chu Y. Simultaneous determination of rivanol and mifepristone in human plasma by a HPLC-UV method with solid-phase extraction. Journal of Chromatography B., 2007; 856: 312- 7.
12. Mattsson C, Bailey MA, Reynolds RM, Walker BR, Andrew R. Quantitative analysis of RU38486 (mifepristone) by HPLC triple quadrupole mass spectrometry. Journal of Chromatography B., 2009; 877: 497-501.
13. Teng Y, Dong R, Wang B, Jiang Z, Wei C, Zhang R, "et al". Determination of mifepristone and its metabolites and their pharmacokinetics in healthy female Chinese subjects. Acta Pharmaceutica Sinica., 2011; 46(10): 1241- 45.
14. Tang C, Zhong G, Chen X, Huang Z, Huang M. Simultaneous determination of mifepristone and monodemethyl-mifepristone in human plasma by liquid chromatography- tandem mass spectroscopy method using levonorgestrel as an internal standard: application to a pharmacokinetic study. Biomedical Chromatography., 2009; 23: 71- 8.
15. Chavan D.D., Damle M.C., Development and validation of stability indicating HPTLC method for estimation of Mifepristone. International Journal of Pharma Research & Review, 2015; 4(4): 13- 9.
16. ICH Q2 (R1), Validation of Analytical Procedures: Text and Methodology, Geneva Switzerland, 2003.