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DEVELOPMENT AND VALIDATION OF DERIVATIVE SPECTROPHOTOMETRIC METHOD FOR ESTIMATION OF MIRABEGRON IN BULK AND TABLET DOSAGE FORM

R. Nageswara Rao[1], Dr. D. Madhuri[1], Dr. L Siva Sanker Reddy[2], K. Rani[1]*, P. Tejaswini[1] and Dr. Kumara Swamy. Gandla[3]

[1]Department of Pharmaceutical analysis & Quality Assurance, Creative Educational Society College of Pharmacy, Chinnatekur, Kurnool. A.P

[2]Department of Pharmaceutical analysis, Santhiram College of Pharmacy, Panyam, Nandyal, A.P

[3]Dept.of pharmaceutical Analysis, Care College of Pharmacy, Oglapur(Vill), Warangal, Telangana.

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***Corresponding Author**
K. Rani
Department of Pharmaceutical analysis & Quality Assurance, Creative Educational Society College of Pharmacy, Chinnatekur, Kurnool. A.P.

ABSTRACT

The present communication deals with development of simple, sensitive, rapid and economical method for estimation of mirabegron in bulk and tablet dosage form. The method of analysis is derivative spectroscopy to eliminate spectral interference by measuring absorbances at 246 nm and 213 nm for Zero order and 1st derivative spectroscopy respectively. It is linear in concentration range of 2-25 µg/ml respectively. The limit of detection (LOD) and limit of quantitation (LOQ) of drug was 0.80 & 0.47 and 2.43 & 1.42 µg respectively. The results of analysis were validated by ICH Q2B (R1). The results of recovery studies and precision were found to be within limits.

KEYWORDS: Mirabegron, Derivative Spectrophotometry and ICHguidlines.

INTRODUCTION

Mirabegron(MBG), Chemically is 2 - (2 – amino - 1, 3 – thiazol – 4 - yl) – N - C4 - (2 - { [(2R) - 2 hydroxy 2 phenylethyl] amino} ethyl)phenyl] acetamide. The empirical formula is $C_{21}H_{24}N_4O_2S$ & the molecular weight is 396.506 g/mol. Mirabegron is a beta-3 adrenergic receptor agonist for the management of overactive bladder. It is an alternative to

antimuscarinic drugs for this indication. By administrating Mirabegron to healthy volunteers orally, the absorption rate reaches maximum concentration around 3.5 hours by administrating 25mg of drug. The absolute bioavailability raises to 29% simultaneously the absolute bioavailability raises to 35% by administering dose of 50 mg. Mirabegron is widely distributed in the body. Majorly metabolisam occurs through different pathways which include dealkylation, oxidation, (direct) glucuronisation, and amide hydrolysis. The majorly observed metabolites in human plasma are phase 2 glucuronides. Pharmacologically these metabolites are inactive towards beta-3 adrenergic receptor. Mirabegron is actively eliminated through tubular secretion followed by glomerular filtration.[1-3] Literature survey[4-11] shown that there are two suitable LC-MS, GC-MS and HPLC methods are available for the determination of mirabegron in common laboratories. The aim of the study was to develop a simple, precise and accurate reverse-phase HPLC method for the estimation of MBG in bulk and pharmaceutical dosage forms. The developed method was validated as per ICH guidelines. The purpose of the present work is develop a simple, rapid, accurate, precise and reproducible RP-HPLC method was developed for the estimation of Mirabegron in tablet dosage form.

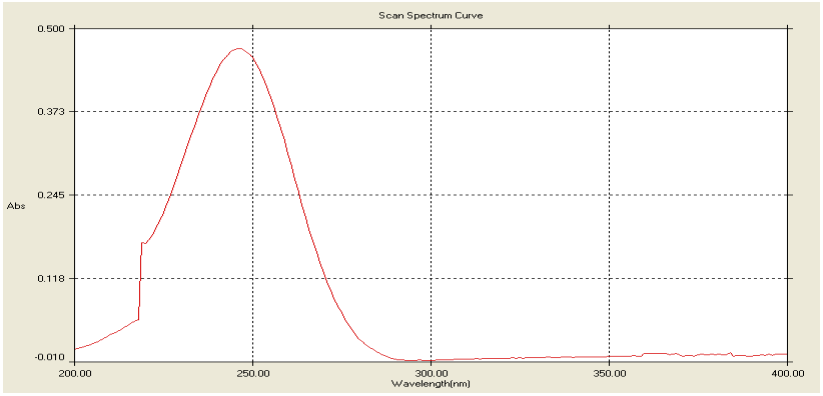
METHODOLOGY

Selection of Solvent: The solubility of mirabegron was determined in a variety of solvents as per Indian Pharmacopoeia standards. Solubility test was carried out in different polar and non-polar solvents from the solubility studies, ethanol and water (1:9) was selected as suitable solvent for proposed method.

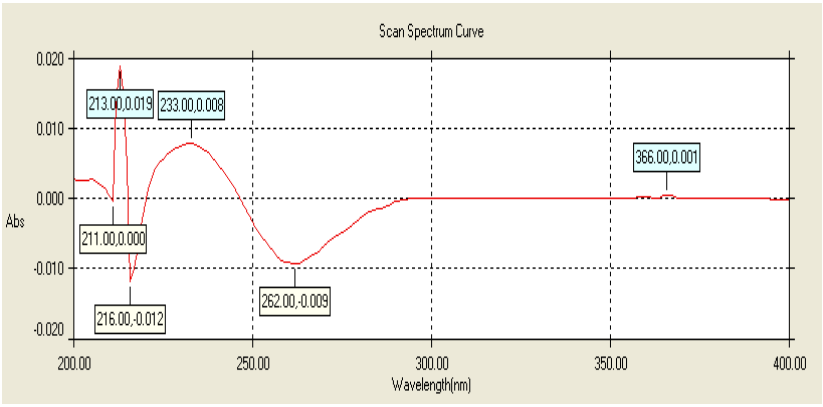
Preparation of Standard Stock Solution: Standard stock solution was prepared by dissolving, accurately measured 10mg of mirabegron in ethanol and water (1:9) and the volume was made up to 10 ml in 10 ml volumetric flask (1^0 stock solution, 1000µg/ml).

Determination of Absorbance Maxima

1ml of 1^0 stock solutions was diluted to 10 ml with ethanol and water (1:9) (2^0 stock solution, 100µg/ml). The absorbance of resulting solution was measured against respective blank solution (distilled water) in the UV region of 200-400 nm, zero order shows maximum absorbance at 246 nm and first order shows maximum absorbance at 213nm.

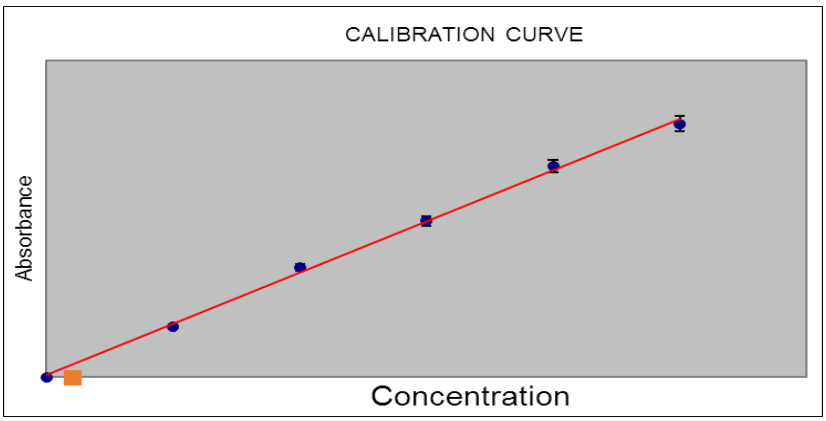


Zero order Ultra violet absorption Spectrum of Mirabegron

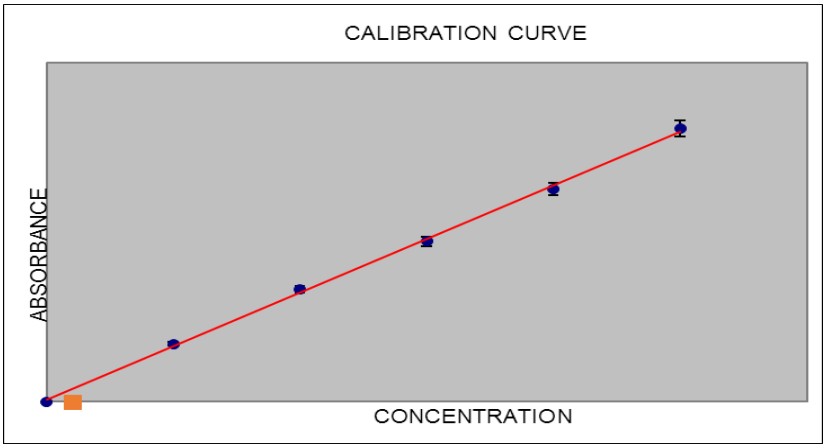


First order Ultra violet absorption Spectrum of Mirabegron

Determination of concentration range: For preparation of different concentrations, aliquots of stock solution of suitable concentrations of mirabegron were transferred into a series of 10 ml standard flasks and volumes were made up to mark with distilled water. Five different concentrations were prepared in the range of 5-25µg/ml and the absorbances were measured at 246 nm and 213 nm against solvent blank. The obtained absorbance values are plotted against the concentrations of mirabegron to get the calibration graph.



Zero order Calibration curve of Mirabegron



Zero order Calibration curve of Mirabegron

Precision: The precision of an analytical method is the degree of agreement among individual test results when the method is applied repeatedly to multiple samplings of homogenous samples.

Intraday and interday precision: A variation of results within the same day (intra – day), variation of results between days (inter- day) was analyzed. Intra – day precision was determined by analyzing mirabegron for six time in the same day at 246 nm and 213 nm. Inter – day precision was determined by analyzing the drug daily once for three days at 246 n and 213 nm.

Interday and Intraday analysis of Mirabegron at 246 nm

S. No.	Interday* (Amount found in µg)	Intraday* (Amount found in µg)
1	15.04	15.27
2	15.09	14.97
3	15.12	15.04
4	15.07	15.05
5	15	15.08
6	15.04	15.02
S.D.	0.0089	0.134
% RSD	0.0085	0.129

*Mean of six observations

Interday and Intraday analysis of Mirabegron at 213 nm.

S. No.	Interday* (Amount found in µg)	Intraday* (Amount found in µg)
1	15.86	16.27
2	15.45	15.04
3	15.65	15.45
4	15.24	15.65
5	15.86	15.86
6	1545	15.24
S.D.	0.0089	0.134
% RSD	0.0085	0.129

Recovery studies: In order to study the accuracy, powder of mirabegron was taken, and used to carry out the analysis. Recovery studies were carried out by addition of standard drug solution (80%, 100% and 120%) to the sample at 3 different concentration levels and the percentage recovery was determined by using the formula.

Percentage Recovery = Amount of drug recovered / Amount of drug added × 100

Recovery studies for the Mirabegron at 246 nm.

S. No.	% added	Amount (µg/ml)	Amount Added (µg/ml)	Amount found	Amount recovered	Avrg % Recovery (x)	Mean ± SD	%RSD
1	80%	15	12	26.7	11.7	99	0.032	0.032
2			12	26.6	11.6			
3			12	26.7	11.7			
4	100%		15	29.9	14.9			
5			15	30.4	15.4			
6			15	30.2	15.2			
7	120%		18	32.1	17.1			
8			18	32.7	17.7			
9			18	33.1	18.1			

Recovery studies for the Mirabegron at 213nm.

S .No	% added	Amount (µg/ml)	Amount Added (µg/ml)	Amount found	Amount recovered	Avrg % Recovery (x)	Mean ± SD	%RSD
1	80%	15 µg/ml	12	26.9	11.9	99.8	0.032	0.032
2			12	26.9	11.9			
3			12	27.1	12.1			
4	100%		15	29.8	14.8			
5			15	30.0	15			
6			15	30.2	15.2			
7	120%		18	32.9	17.9			
8			18	32.9	17.9			
9			18	33.2	18.2			

Limit of Detection (LOD) and Limit of Quantification (LOQ):

Preparation of calibration curve from the serial dilutions of standard was repeated for six times. The limit of detection and limit of quantification was calculated by using the average value of slope and standard deviation of intercept.

RESULTS AND DISCUSSION

Optical characteristics of Mirabegron

Parameters	Values	
	Zero order	First order
λ_{max}(nm)	246	213
Beers Law limits (µg / ml)	5-25	5-25
Regression equation (Y)	Y= 0.0041X + 0.003	Y= 0.0048X + 0.001
Slope (m)	0.041	0.048
Intercept (C)	0.003	0.001
Correlation coefficient (r^2)	0.0998	0.998
Limit of Detection (µg / ml)	0.80	0.470
Limit of Quantitation (µg/ ml)	2.43	1.424

An effort has been made to develop a simple, accurate method to estimate mirabegron in bulk and pharmaceutical preparation and to validate the method, according to ICH Q2 (R1) guidelines.

The absorbance maxima for zero order and first order were recorded at wavelength of 246nm and 213nm which is shown in fig 1 and fig 2. Beers law range was confirmed by linear curve of mirabegron. Linearity for mirabegron is shown in fig: 3&4.

From the above studies the optical characteristics such as linearity range (5-25µg/ml), correlation coefficient (0.998 & 0.998), slope (0.041 & 0.00048) and intercept (0.003 & 0.001) were calculated and results were found to be satisfactory. Quantitative data subjected to statistical analysis. The % RSD values < 2 indicate the precision of methodology.

The accuracy was confirmed by recovery studies by adding known amount of pure drug to the previously analyzed formulation and the mixture was analyzed by the proposed method was found to be 100.15 & 98.89 %. The values are given in recovery was confirmed and shown in the table: 5.

SUMMARY AND CONCLUSION

Estimation of mirabegron was achieved by UV method. After considering the solubility and stability, Ethanol and water (1:9) was selected as solvent. Mirabegron 10µg/ml solution was

prepared and scanned in the uv-region. The absorbance maxima for zero order and first order were 246 and 213nm which was selected as an analyzing wavelength.

Calibration curve was plotted by using concentration Vs absorbance. From the calibration curve it was found that mirabegron obeys beer's law in the range of 5-25µg/ml, the precision of the method was studied by making repeated analysis. The recovery studies were also carried out to ensure the accuracy of the method by adding known concentration of pure drug to a preanalysed formulation.

All the above parameters combined with simplicity and ease of operation ensures that the application of proposed method from UV Spectrophotometric method for estimation of mirabegron was found to be useful with high accuracy, precision. It can be used for routine analysis of mirabegron in bulk and pharmaceutical preparation.

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