K. Sujana et al /J. Pharm. Sci. & Res. Vol.3(4), 2011,1122-1126

ISSN:0975-1459
Journal of Pharmaceutical Sciences and Research
www.jpsr.pharmainfo.in

Difference Spectrophotometric Methods for Pioglitazone Hydrochloride and Metformin Hydrochloride

K.Sujana, K.Abbulu, O.Bala Souri, B.Archana, M.Sindu, G.Swathi Rani
Department of Pharmaceutical Analysis, Acharya Nagarjuna University, Nagarjuna nagar-522510.

Abstract
Difference spectrophotometric method was developed for the estimation of Pioglitazone and Metformin in bulk drug and in pharmaceutical formulations. Difference spectrum obtained, by keeping Pioglitazone and Metformin separately in 0.1M NaOH in sample cell and 0.1M HCl as blank, showed characteristic peaks(λ_{max}) at 228.1nm (PIO) and 228.2nm (MET) and the characteristics peaks for pharmaceutical formulations were also found. This was depicted by plotting the graphs between wavelength and absorbance. Difference of absorbance between these two maxima was calculated to find out the amplitude, which was plotted against concentration. The optical characteristics for this method are precise and accurate. The proposed method can be applied to pharmaceutical formulations and the common excepients present in the formulation did not interfere with proposed method. The results indicate that the method is simple, sensitive and can be used for routine estimation of Pioglitazone and Metformin in pharmaceutical dosage form.
Keywords: Difference spectrophotometry, Metformin, Pioglitazone

INTRODUCTION:

Pioglitazone and Metformin are the two new anti-diabetic drugs and chemically Pioglitazone is [(±)-5-[[4-[2-(5-ethyl-2-pyridinyl) ethoxy] phenyl] methyl]-2,4-] thiazolidinedione monohydrochloride and Metformin is *(N,N*-dimethylimidodicarbonimidic diamide hydrochloride) . The main use for Pioglitazone and Metformin is in the treatment of diabetes mellitus type 2, especially in overweight people. Difference spectrophotometry of Pioglitazone and Metformin were not revealed in literature. An attempt in the present study has been made to develop simple, accurate and economical method for difference spectroscopy of Pioglitazone and Metformin and their pharmaceutical formulations. The result of analysis using the developed spectrophotometric methods for difference spectrophotometry was found to be satisfactory such that the developed methods can be used for routine analysis of drugs and pharmaceutical dosage form.

MATERIALS AND METHODS

Apparatus

Spectral & absorbance measurements were made on ELICO UV-Visible spectrophotometer using 10mm Quartz matched cells with wavelength readability 0.1 nm increment was employed for all measurements. The absorption spectrum was recorded in the wavelength range of 200-400nm throughout the experimental work.

Reagents and solutions:

Pioglitazone hydrochloride (PIO) and Metformin hydrochloride (MET) were gifted by and Matrix and Aurobindo Pharmaceuticals respectively. Double distilled water was prepared in the laboratory.

Preparation of Solvents:

0.1M NaOH:
2 gms of NaOH was accurately weighed and dissolved in double distilled water and the volume was made up to 50ml with double distilled water.

0.1M HCl:
4.25ml of HCl was made up to 50ml with double distilled water.

Phosphate Buffer PH-7:
0.025gm of anhydrous disodium hydrogen phosphate and 0.0150gm of potassium dihydrogen phosphate was accurately weighed and dissolved in double distilled water and the volume was made upto 50ml with distilled water.

Preparation of standard stock solution:

Accurately weighed 0.01gm (10mg) of PIO & MET was dissolved in 10ml of ethanol in two separate standard volumetric flasks to get 1mg/ml.

PROCEDURE:

For bulk samples:

From the standard solutions, 1ml of solution was taken out and made up to 10ml with ethanol and again from this 1ml was taken and made up to 10ml with NaOH. From this 0.01, 0.02, 0.03, 0.04, 0.05 ml of aliquots of solution were transferred into a series of 10ml volumetric flasks and volume was made up to 10ml with NaOH. The amounts of PIO & MET present in the sample were computed from their calibration curves (using HCl as blank).Fig. vii and viii.

For pharmaceutical preparations:

An accurately weighed tablet powder of equivalent to 15mg of PIO & MET was dissolved in 10ml of ethanol and filtered using Whatmann filter paper. From the filtered solutions, 1ml of each was taken and made up to 10ml with NaOH and the absorbance was checked using HCl as blank and the λmax of pure drugs and formulations are plotted in Fig.iii and iv.

Spectral Characteristics:

In order to ascertain the optimum wavelength of the species formed, the spectra was scanned on a UV-Visible spectrophotometer in the range of 200-400nm.λmax of acid, base and buffer was found separately. The base absorption spectra was identical with buffer, hence acid (HCl) was used as a blank for base (NaOH) as PIO & MET is basic in nature, base wavelength was higher than acid as shown in Fig:i & ii.This is because the absorption spectrum of PIO & MET in acid medium shows hypsochromic shift and hypochromic effect.

The absorption spectrum of PIO & MET was measured by the absorbance of equimolar PIO & MET solutions. The λmax of PIO & MET was found to be 228.1nm and 228.2nm respectively as shown is Fig.v and vi.

Fig.i.Absorbance maxima of PIO

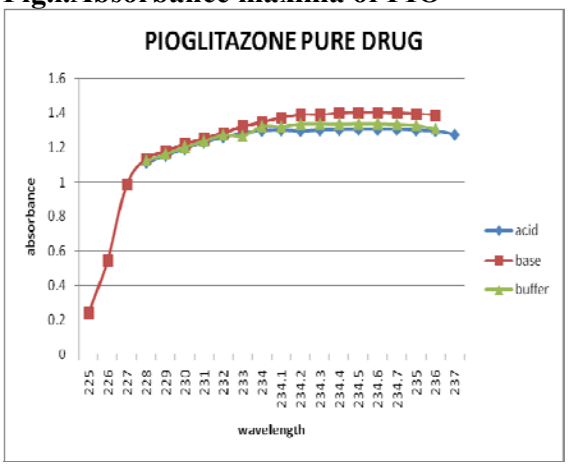


Fig.ii.Absorbance maxima of MET

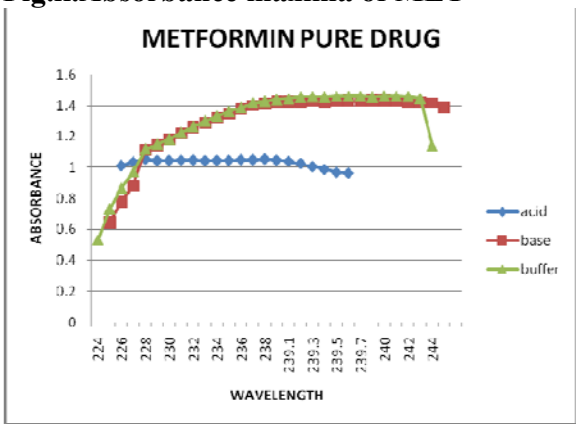


Fig.iii.Absorbance maxima of PIO pure drug and Formulations

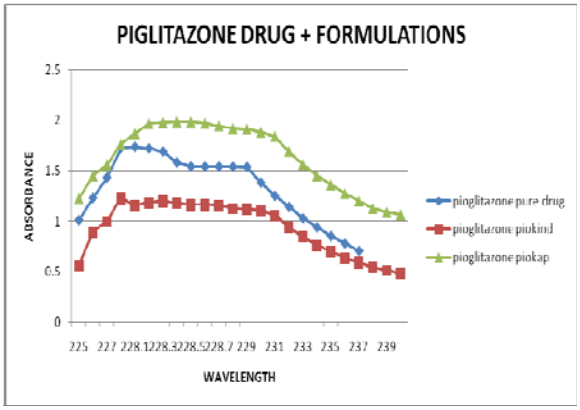


Fig.iv.Absorbance maxima of MET pure drug and Formulations

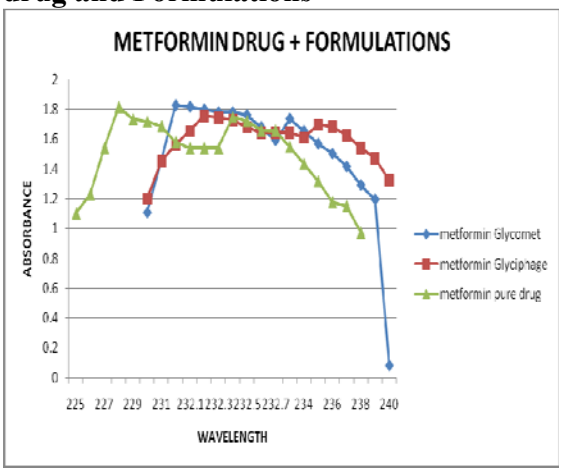


Fig.v.λmax of PIO

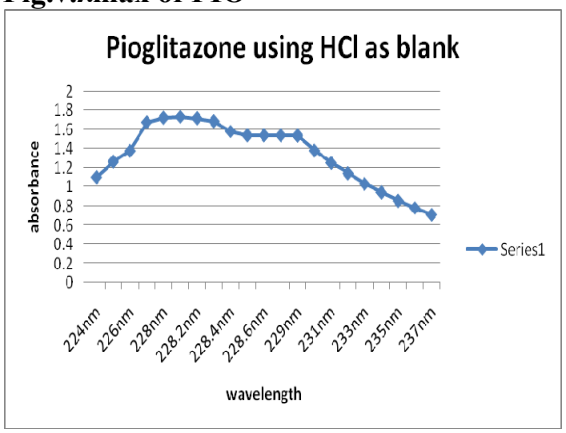


Fig.vi.λmax of MET

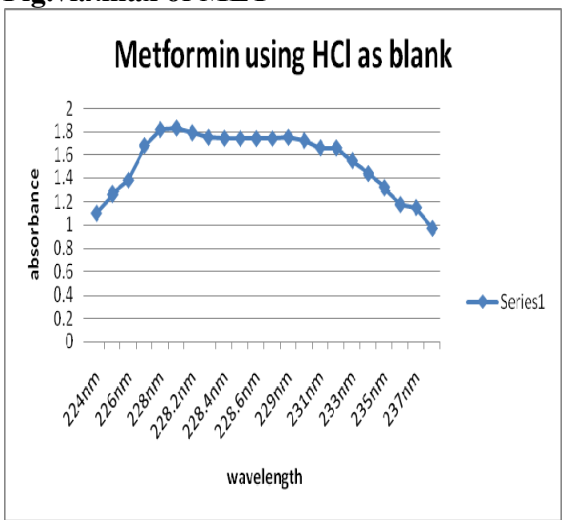


Fig.vii.Calibration of PIO

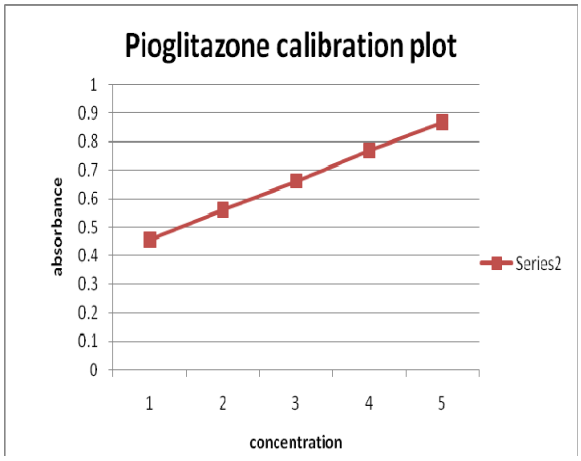
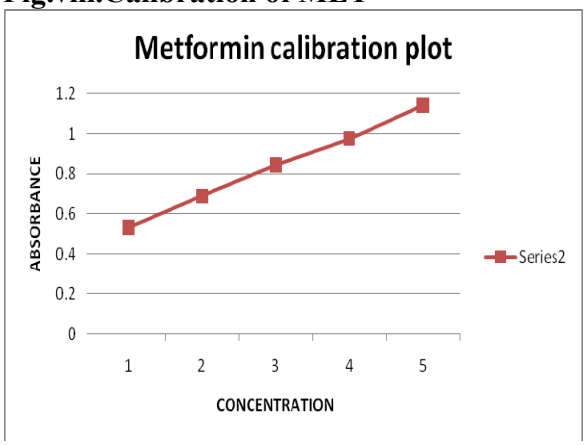


Fig.viii.Calibration of MET



Sensitivity of the method:

For finding the Beer's limit of the method, the absorbance for a set of solutions containing varying amounts of PIO & MET was measured at 228.1nm and 228.2nm against blank with UV-visible spectrophotometer. The linearity plot between absorbance and concentration of PIO & MET showed that the system obeys Beer's law.

Precision of the method:

The precision of the method was established by carrying out the analysis of the analytes (n=8) using the proposed developed methods. The low value of % Relative standard deviation showed that the methods were precise. The results are shown in Table. No.1 for PIO & MET.

Accuracy of the method:

To check the accuracy of the developed methods and to study the interference of formulation excipients, analytical recovery experiments were carried out by using standard addition method at 50, 100, 150% levels. From the total amount of drug found, the percentage recovery was calculated. The results revealed no interference of excipients. The results of recovery studies were summarized in Table -2 for PIO & MET.

Optical characteristics such as Beer's law limits, molar extinction coefficient, correlation coefficient and regression equation, % relative standard deviation (calculated from eight measurements containing $3/4^{th}$ of the amount of upper Beer's law limits) were calculated and results are shown in Table -1 for PIO & MET.

Table - 1: Optical characteristics of Pioglitazone and Metformin

Parameters	Pioglitazone	Metformin
Beer's law limit (µg/ml)	0.1-0.5	0.1-0.5
λmax(nm)	228.1nm	228.2nm
Molar absorptivity (L mole^-1 cm^-1)	77.566*10	57.049*10
Regression equation (y=b+aC)	Y= (-0.25) + 0.65C	Y=(-0.41) + 0.830C
Slope (b)	-0.25	-0.41
Intercept (a)	0.657	0.830
Correlation coefficient (r)	1.0	0.999
*Relative standard deviation (%)	0.52886	0.2790

Y= b+aC, where 'C' is the concentration in mg/ml and 'Y' is the absorbance.

* calculated from eight replicate samples.

Table - 2: Recovery Studies of Pioglitazone and Metformin:

Commercial sample	**% Recovery of PIO	**% Recovery of MET
Brand 1	98.0	99.8
Brand 2	101.3	100.8

** Recovery amount was the average of 3 determinations.

RESULTS AND DISCUSSION

The proposed method is based on difference spectrophotometric estimation of PIO & MET in UV region using ethanol as solvent. The absorbance spectral analysis shows the maximum absorbance at 228.1nm for PIO and 228.2nm for MET. The correlation coefficients were found to be in between 0.999-1.0 which shows the good linear relationship for both components. The results of optical characteristics such as Beer's law limits, correlation coefficient, slope, intercept and absorptivity coefficient values were summarized in Table-1.

The tablet assay results obtained by proposed methods were very close to labeled claim and low value of standard deviation, suggesting that the developed methods has high precision. In order to check the accuracy of the developed methods, known quantities of standard drugs of PIO & MET at three different levels were added to its preanalyzed tablet sample and analyzed by the developed methods. The results of recovery studies are shown in Table-2. The mean percentage recoveries were found in the range of 98.0-101.3 shows no interference of the excipients in the tablet formulation.

CONCLUSION

The data and information concerning drugs, reagents and techniques given in results and discussion reveal that the proposed methods are simple, selective, sensitive (some are superior to the other methods) and accurate with reasonable precision. In addition, selectivity to each selected drug in its formulations was achieved by selecting the appropriate combination of solvent systems, acids or bases in sample solution preparation and exploiting specific functional groups exclusively present in the drug but not in the excepients, additives or other active ingredient present in the formulations, to the extent possible. The proposed methods can be used as alternative methods to reported ones and provide a wide choice for the routine determination of the above mentioned drugs depending upon the availability of chemicals and situation arising due to the presence of concomitants. The proposed method is simple, sensitive, precise and accurate and can be used for routine estimation of Pioglitazone and Metformin in pharmaceutical dosage form.

ACKNOWLEDGEMENTS

Authors are thankful for the Matrix and Aurobindo Pharmaceuticals for providing the gift samples of drugs Pioglitazone and Metformin.

REFERENCES

1. *Indian Pharmacopoeia*, Government of India Ministry of Health and Family Welfare, Indian Pharmacopoeia Commission, Ghaziabad 3, 1674 (2007).
2. *United states Pharmacopoeia* 30 NF 25 "The official compendia of standards, Asian edition, 2007, *vol: 1.*
3. *ICH Guidelines Q2BValidation of Analytical Procedures*: Methodology (1996)
4. A.H.Beckett, J.B.Stenlake, PracticalPharmaceutical *chemistry*, IV-Edition, part two, CBS Publishers and distributors, 2004, p.no.326.
5. Dunge, N. Sharda, B. Singh and S. Singh, *J. Pharm.Biomed. Anal.*, 2005, *37*, 1109.
6. B. M. Rao, M. K. Srinivasu, G. Sridhar, P. R. Kumar,K. B. Chandrasekhar and A. Islam, *J. Pharm. Biomed. Anal.*, 2005, *39*, 503.
7. L. Huber and S. George, eds., *"Diode-array detection in HPLC",* New York, Marcel Dekker, 1993.
8. L. Huber, *"Validation and qualification in analytical laboratories",* Interpharm, 2002.
9. R.T. Sane, S.N. Menon, Shafi Inamdar , Mandar Mote and Gunesh Gund, Simultaneous Determination of Pioglitazone and Glimepiride by High-Performance iquid Chromatography , Chromatographia 2004, 451-453.
10. P. K. Sahoo, R. Sharma,* and S. C. Chaturvedi, Simultaneous Estimation of Metformin Hydrochloride and Pioglitazone Hydrochloride by RPHPLC Method from Combined Tablet Dosage Form*, Indian J Pharm Sci.* 2008 May–Jun; *70*(3): 383–386