RESEARCH ARTICLE

Spectrophotometric estimation of pioglitazone hydrochloride in tablet dosage form

Pawan K Basniwal, Prabhat K Srivastava[1], Deepti Jain[2]

L.B.S. College of Pharmacy, Jaipur, Rajasthan, India, [1]Department of Pharmaceutics, Banaras Hindu University, Varanasi, UP, India, [2]School of Pharmaceutical Sciences, Rajiv Gandhi Technical University, Bhopal, MP, India

Two simple, rapid, and precise methods - linear regression equation (LRE) and standard absorptivity - were developed and validated for the estimation of pioglitazone hydrochloride in tablet dosage form. The maximum absorbance (λ_{max}) of pioglitazone hydrochloride was found to be 269.8 nm in methanol:water:hydrochloric acid (250:250:1). Beer-Lambert law was obeyed in the concentration range of 10-50 µg/ml, and the standard absorptivity was found to be 253.97 dl/g/cm. Both the methods were validated for linearity, accuracy, precision (days, analysts, and instrument variation), and robustness (solvent composition). The numerical values for all parameters lie within the acceptable limits. Pioglitazone hydrochloride was estimated in the range of 99.58-99.97% by LRE method and 100.25-100.75% by standard absorptivity method. At 99% confidence limit, the F-test value for the methods was found to be 1.8767.

Key words: *Linear regression equation, standard absorptivity, pioglitazone hydrochloride, spectrophotometric estimation*

INTRODUCTION

Pioglitazone hydrochloride, chemically [(±)-5-[[4-[2-(5-ethyl-2-pyridinyl)ethoxy]phenyl] methyl]-2, 4] thiazolidine-dione monohydrochloride, is thiazolidine-dione derivative that highly selective agonist for peroxisome proliferator-activated receptor gamma (PPAR) and is used as an adjunct to diet to improve glycemic control in patient with type 2 diabetes (non-insulin-dependent diabetes mellitus). The literature survey reveals that chromatographic methods are reported for simultaneous estimation of pioglitazone and its metabolites in human plasma, human serum, and urine. There is also simultaneous estimation of pioglitazone and glimpiride by chromatographic method, but no spectrophotometric is yet reported.[1-6] Present work deals with the development of two spectrophotometric methods - linear regression equation (LRE) and standard absorptivity - and the validation of these developed methods according to the ICH guidelines to estimate pioglitazone hydrochloride in dosage form.

MATERIALS AND METHODS

Materials

UV1700 series (Shimadzu, Japan) and UV vis double beam spectrophotometer 2201 (Systronic, Ahemadabad) were used for work working standard of pioglitazone was gift sample from Aristo Pharmaceuticals (Mandideep, MP, India) and tablets were procured from the local market (Pioglar-15; Ranbaxy Laboratory Ltd., Goa). Methanol (AR grade) and hydrochloric acid were from Merck Limited (Mumbai, India).

Linear regression equation method

Accurately weighed about 100 mg of pioglitazone hydrochloride was dissolved in 100 ml solvent system (methanol:water:hydrochloric acid = 250:250:1) to obtain 1000 µg/ml concentration of drug (stock A). Stock A (10 ml) was diluted up to 100 ml with solvent system to obtain 100 µg/ml concentration (Stock B). Aliquots of Stock B were diluted to obtain concentrations of 10, 20, 30, 40, and 50 µg/ml of pioglitazone hydrochloride. All dilutions were scanned from 300 to 200 nm against solvent system as blank [Figure 1] and their absorbance were observed at 269.8 nm [Figure 2]. The LRE was developed as ABC = 0.0256C + 0.000, where ABC = absorbance and C = concentration of dilutions in µg/ml, with the correlation coefficient r^2 = 0.9998.

Standard absorptivity method

Five dilutions were prepared in triplicate and the absorbance was observed at 269.8 nm. The standard absorptivity A (1%, 1 cm) and molar extinction coefficient ε were calculated from the above observations [Table 1].

Validation

As per the ICH guidelines,[7,8] six dilutions in three

Address for correspondence:
Pawan K. Basniwal, L.B.S. College of Pharmacy, Jaipur, Rajasthan, India.
E-mail: pawanbasniwal@gmail.com

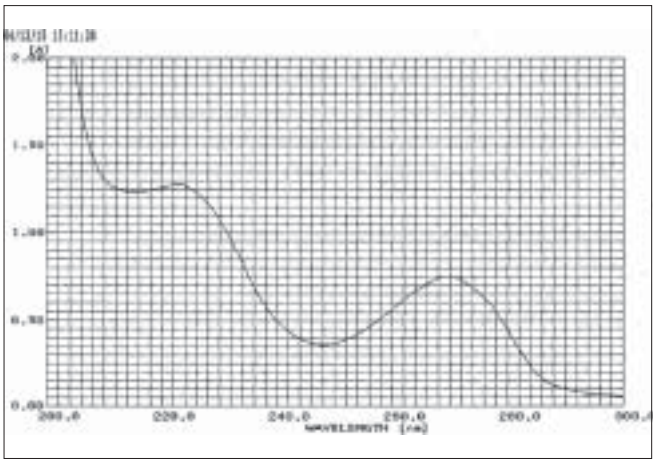

Figure 1: Gaussian spectra of Pioglitazone hydrochloride in method: Water: HCL (250:250:1) solvent system

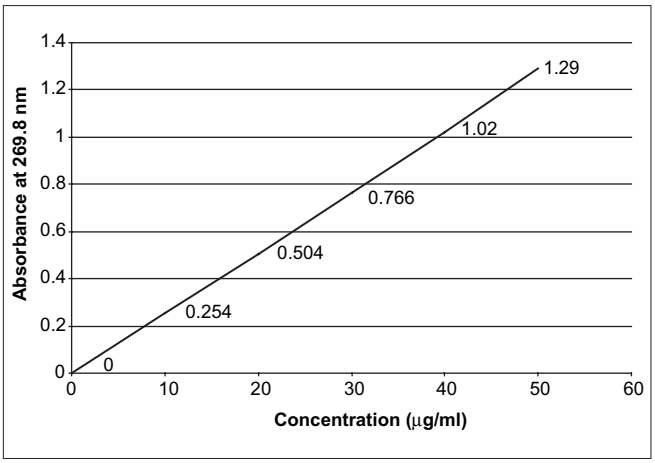

Figure 2: Calibration graph of Pioglitazone hydrochloride

Table 1: Standard absorptivity A (1%, 1 cm) and molar extinction coefficient ε

Concentration (µg/ml)	Absorbance of triplicates at 269.8 nm			Standard absorptivity A (1%, 1 cm) = A/bc		
	I	II	III	I	II	III
10	0.254	0.250	0.248	254.0	250.0	248.0
20	0.504	0.500	0.502	252.0	250.0	251.0
30	0.766	0.765	0.760	255.3	255.0	253.3
40	1.020	1.025	1.021	255.0	256.3	255.3
50	1.290	1.288	1.292	258.0	257.6	258.4
Standard absorptivity A (1%, 1 cm)				A (1%,1 cm) = 253.97 dl/g/cm		
Molar extinction coefficient				ε = 9978.35 1/mol/cm		

replicates were used to validate the methods for linearity, accuracy (by recovery studies), repeatability, intermediate precision (days, analysts, and instruments), robustness, and statistical parameters were calculated [Table 2].

Assay of tablets

Twenty tablets were weighed and finely powdered. Powder equivalent to 100 mg of pioglitazone hydrochloride was dissolved in 50 ml methanol by heating on water bath at 40°C for 30 min and volume made up to 100 ml with solvent system. Solution was filtered through Watmann paper no. 41 to obtain stock P. Stock P (10 ml) was diluted to obtain stock Q and aliquots of it were diluted to get sample concentrations in the range of linearity. Concentrations of sample solution were observed in multipoint calibration curve of quantitative mode at 269.8 nm by LRE method. Concentrations of sample solution were also calculated by using standard absorptivity [(1%, 1 cm) = 253.97 dl/g/cm and molar extinction coefficient (ε = 9978.35 l/mol/cm) [Table 3].

RESULTS AND DISCUSSION

In 50% aqueous methanol, pioglitazone hydrochloride gives zig-zag spectra and on the addition of hydrochloric acid it shift to characteristic Gaussian spectra accompanying

Table 2: Validation parameters

Parameters	LRE method	SA method
Linearity	10-50 µg/ml	10-15 µg/ml
Response ratio	0.0255	0.0254
SD of RR	0.0002	0.0002
Range	20-40 µg/ml	20-40 µg/ml
SD	0.0002	0.0002
Accuracy		
% Mean	99.71	100.24
SD	0.58	0.75
Precision repeatability		
% Mean	99.84	100.22
SD	0.30	0.13
Intermediate precision		
Day	99.58	100.06
% Mean	0.38	0.11
SD		
Analyst		
Mean	99.54	100.22
SD	0.36	0.33
Instrument		
% Mean	99.6	100.4
SD	0.45	0.45
Robustness		
% Mean	99.6	100.39
SD	0.51	0.52

LRE = Linear regression equation; SA = standard absorptivity; SD = standard deviation; RR = response ratio

Table 3: Assay of pioglitazone hydrochloride tablets

S. No	% Concentration found*		*t*-test	F-test
	LRE method	SA method		
1	99.58	100.25		
2	99.83	100.68	3.9636	1.8767
3	99.97	100.75		
Mean	99.793	100.560		
SD	0.1976	0.2707		

*Mean of six replicates; LRE = linear regression equation; SA = standard absorptivity; SD = standard deviation

accessible pattern for pioglitazone hydrochloride. For complete extraction of drug from tablet dosage form, methanol solution was heated on water bath at 40°C for 30 min. Pioglitazone hydrochloride was estimated within 99.58-99.97% with 0.1976 standard deviation by LRE method. By standard absorptivity method, it was estimated within 100.25-100.75% with 0.2707 standard deviation. The calculated value of F (1.8767) is very less than the theoretical value at 99% confidence limit; thus, the methods have comparable precisions.

Hence, the developed methods for pioglitazone hydrochloride are quite simple, rapid, and economical with acceptable limits of accuracy, precision, reproducibility, and robust to slight variation in experimental conditions. Therefore, methods may be useful for routine analysis of pioglitazone hydrochloride as bulk drug, in dosage form and dissolution studies in pharmaceutical industries.

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