International Journal of Pharmaceutics and Drug Research
ISSN: 2347-6346
Available online at http://ijpdr.com

Original Research Article

UV METHOD DEVELOPMENT FOR ALOGLIPTIN & PIOGLITAZONE USING HYDROTROPIC PHENOMENON

Vikky Dawar*, Ankit Diwan, Kuldeep Ganju
Sagar Institute of Pharmacy & Technology (SIPTec), Gandhi Nagar, Bhopal, 462036 (M.P.)

***Correspondence Info:**
Vikky Dawar
Sagar Institute of Pharmacy & Technology (SIPTec), Gandhi Nagar, Bhopal, 462036 (M.P.)
Email:
bhavikadawar1996@gmail.com

***Article History:**

Received: 02/07/2025
Revised: 21/08/2025
Accepted: 13/08/2025

ABSTRACT

Alogliptin (AGT) and Pioglitazone (PGZ) are widely used in combination therapy for the management of type 2 diabetes mellitus. Developing a simple and economical analytical method for their simultaneous estimation is essential for quality control of pharmaceutical formulations. The present work aimed to develop and validate a UV spectrophotometric method for the simultaneous estimation of AGT and PGZ using the hydrotropic phenomenon, following ICH guidelines. A UV method was developed employing hydrotropic solubilization to enhance the aqueous solubility of AGT and PGZ. The method was validated for linearity, accuracy, precision, repeatability, and reproducibility. Linearity was evaluated in the concentration range of 5–25 µg/ml for both drugs. Accuracy was determined through recovery studies at three levels (80%, 100%, 120%). Precision was assessed by intra-day, inter-day, and analyst-to-analyst variation studies. The validated method was applied for assay of marketed combined tablet formulation. The developed method showed excellent linearity with correlation coefficients of 0.9997 for AGT and 0.9998 for PGZ. %Recovery ranged from 98.24–98.85% (AGT) and 97.64–98.51% (PGZ), confirming method accuracy. Precision studies yielded %RSD values below 2%, indicating good reproducibility. The assay results for marketed tablets were 99.40% (AGT) and 99.17% (PGZ) of label claim, meeting pharmacopeial requirements. The developed UV spectrophotometric method using hydrotropic phenomenon is simple, accurate, precise, and cost-effective. It can be successfully applied for routine quality control analysis of Alogliptin and Pioglitazone in bulk and pharmaceutical dosage forms, offering a greener and economical alternative to chromatographic methods.

Keywords: Alogliptin; Pioglitazone; UV Spectrophotometry; Hydrotropic Solubilization; Method Validation; Linearity; Precision; Accuracy; Quality Control.

INTRODUCTION

Combination therapy has become a cornerstone in the management of type 2 diabetes mellitus, as it helps in achieving better glycemic control and reducing long-term complications. Alogliptin is a selective dipeptidyl peptidase-4 (DPP-4) inhibitor that increases incretin hormone levels, thereby enhancing insulin secretion and decreasing glucagon levels (Nakahara *et al.*, 2011). Pioglitazone, a thiazolidinedione, acts as a peroxisome proliferator-activated receptor-γ (PPAR-γ) agonist, improving insulin sensitivity in adipose tissue, liver, and skeletal

muscle (Soccio *et al.,* 2014). The combination of these two drugs is widely prescribed for the management of type 2 diabetes mellitus, necessitating the development of simple and reliable analytical methods for their simultaneous estimation in bulk and dosage forms.

Chromatographic methods such as HPLC have been widely reported for the determination of alogliptin and pioglitazone, either individually or in combination (Chaudhari *et al.,* 2015; Sharma *et al.,* 2018). However, HPLC methods require expensive instrumentation, high-purity solvents, and longer analysis time. UV-visible spectrophotometry, on the other hand, provides a simple, cost-effective, and rapid alternative for routine analysis (Mahaparale *et al.,* 2020).

One of the major limitations of UV spectrophotometry is the poor aqueous solubility of drugs such as pioglitazone, which can affect linearity and reproducibility. To overcome this limitation, hydrotropic solubilization can be employed. Hydrotropy refers to the phenomenon by which the aqueous solubility of poorly soluble compounds is enhanced in the presence of large concentrations of hydrotropic agents such as sodium benzoate, sodium salicylate, or urea (Crammer *et al.,* 1982). Several researchers have successfully used hydrotropy to develop UV spectrophotometric methods for poorly water-soluble drugs, demonstrating good linearity, accuracy, and precision without the use of organic solvents (Maheshwari *et al.,* 2006; Rajput *et al.,* 2011).

The objective of the present work is to develop and validate a simple, accurate, and precise UV spectrophotometric method for simultaneous estimation of alogliptin and pioglitazone in bulk and pharmaceutical dosage forms using hydrotropic solubilization. The method will be validated as per ICH guidelines for linearity, precision, accuracy, specificity, robustness, and sensitivity (ICH, 2005).

MATERIALS AND METHODS

Materials

Alogliptin (AGT) and Pioglitazone (PGZ) pure drug samples were obtained as gift samples from a reputed pharmaceutical industry. Marketed combined tablet formulation containing AGT (25 mg) and PGZ (30 mg) was procured from a local pharmacy. Analytical-grade chemicals and reagents, including hydrotropic agents, methanol, and distilled water, were used throughout the study. All chemicals and solvents were of analytical grade and used without further purification. UV spectrophotometric analysis was performed using a double-beam UV–Visible spectrophotometer with matched quartz cuvettes.

Methods

Solubility

Solubility of AGT and PGZ was determined at 25±1°C. Accurately weighed 10mg AGT and PGZ was added in different 10 ml volumetric flask containing different solvent and placed at mechanical shaker for 8 hrs. After 8 hrs filter both solution were filtered through whatman filter paper No. 41. The filtrates were diluted suitably and analyzed visually.

Determination of Solubility Enhancement by UV VIS. Spectroscopy

The solubility enhancement study of Alogliptin (AGT) and Pioglitazone (PGZ) in

various solvents and solvent systems revealed significant variation depending on the solvent used. Water served as the baseline with a fold value of 1 for both drugs. Both drugs exhibited a slight increase in solubility in hot water, indicating that temperature can modestly improve dissolution, likely due to increased molecular mobility and reduced solvent viscosity.

Selection of solvent system

AGT and PGZ were scanned in various hydrotropic agent in the spectrum mode over the UV range (200-400) and 2M Ammonium Acetate: 2M Sod. Citrate (1:1) was found to be most appropriate

Linearity range and calibration graph

Preparation of Standard and Working Solutions for AGT and PGZ

Preparation of Standard Stock Solution (Stock-A):

Standard stock solutions were prepared by dissolving 10 mg of each drug separately in 8 mL of a mixed hydrotropic solution containing 2M Ammonium Acetate and 2M Sodium Citrate in a 1:1 ratio. The solutions were sonicated for 10 minutes to ensure complete solubilization of the drugs, and the volume was then adjusted to 10 mL with the same mixed hydrotropic solution to obtain a concentration of 1000 µg/mL (Stock-A) for both AGT and PGZ.

Preparation of Sub-Stock Solution (Stock-B):

From Stock-A, 1 mL aliquots of AGT and PGZ were withdrawn using a pipette and transferred into separate 10 mL volumetric flasks. Each was diluted up to 10 mL with distilled water, resulting in a concentration of 100 µg/mL (Stock-B) for both drugs.

Preparation of Working Standard Solutions:

For AGT: Aliquots of 0.5, 1.0, 1.5, 2.0, and 2.5 mL were withdrawn from Stock-B and transferred into 10 mL volumetric flasks. Each flask was then diluted up to 10 mL with RO water to obtain working solutions of 5, 10, 15, 20, and 25 µg/mL, respectively.

For PGZ: Similarly, 0.5, 1.0, 1.5, 2.0, and 2.5 mL aliquots were withdrawn from Stock-B, transferred into 10 mL volumetric flasks, and diluted up to 10 mL with RO water to achieve concentrations of 5, 10, 15, 20, and 25 µg/mL, respectively (Rane *et al.,* 2015).

Selection of Wavelength for Linearity:

Solutions of 10 µg/mL of AGT and PGZ were prepared separately and scanned in spectrum mode over the range of 200–400 nm. The maximum absorbance was observed at 276 nm for AGT and 224 nm for PGZ. Both drugs demonstrated linearity in the concentration range of 5–25 µg/mL at their respective λ_{max} values. Calibration curves were plotted with absorbance versus concentration to confirm linearity (Maheshwari *et al.*, 2010).

The selected wavelengths for further linearity and analytical studies were 276 nm for AGT and 224 nm for PGZ.

Selection of wavelength for linearity

Solutions of 10µg/ml of AGT and 10µg/ml PGZ were prepared separately. Both the solutions were scanned in the spectrum mode from 200 nm to 400 nm. The maximum absorbance of AGT and PGZ was observed at 276.0 nm and 224.0 nm, respectively.

AGT and PGZ showed linearity in the concentration range of 5-25µg/ml and 5-25µg/ml at their respective maxima (Maheshwari *et al.,* 2010). Calibration curve was plotted, absorbance versus concentration.

To study the linearity of AGT and PGZ the selected wavelength are:

Method (Simultaneous equation method)

Study of overlay spectra

Working standard solution from the standard stock solution prepared in concentration 10µg/ml of AGT and 10µg/ml of PGZ were scanned in the spectrum mode over the range of 200-400 nm against RO Water as blank and the overlain spectra of the two were recorded. AGT showed an absorbance peak at 256.0 nm, whereas PGZ at 232.0 nm. The overlain spectra also showed isoabsorptive points at 240.0 nm. Due to difference in absorbance maxima and having no interference with each other so both drug can be simultaneously estimated by simultaneous equation method (Khan, 2015).

Simultaneous equation method is based on the absorption of drugs (X and Y) at the wavelength maximum of the other. Two wavelengths selected for the method are 276.0 nm and 224.0 nm that are λ_{max} of AGT and PGZ respectively. The absorbances were measured at the selected wavelengths and absorptivities ($A^{1\%,\ 1cm}$) for both the drugs at both wavelengths were determined as mean of five independent determinations. Concentrations in the sample were obtained by using following equations:

$$C_{TGL} = \frac{A1ay2 - A2ay2}{ax1ay2 - ax2ay1} \ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots Eq.(1)$$

$$C_{PGZ} = \frac{A1ax2 - A2ax2}{ax1ay2 - ax2ay1} \ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots Eq.(2)$$

Where, A_1 and A_2 are absorbances of mixture at 276.0 nm and 224.0 nm respectively, ax_1 and ax_2 are absorptivities of AGT at λ_1 (276.0 i.e. λ_{max} of AGT) and λ_2 (224.0 i.e. λ_{max} of PGZ) respectively and ay_1 and ay_2 are absorptivities of PGZ at λ_1 and λ_2 respectively. C_{PGZ} and C_{AGT} are concentrations of AGT and PGZ respectively. The overlain spectra of both the drugs in 25:30 ratio and the criteria for obtaining maximum precision [i.e. absorbance ratio $(A_2/A_1)/ax_2/ax_1$ and ay_2/ay_1] by this method were calculated and found to be outside the range of 0.1-2.0 which is satisfied for both the AGT and PGZ.

Validation of simultaneous equation method

Linearity

Linearity of both drugs was established by response ratios of drugs. Response ratio of drug calculated by dividing the absorbance with respective concentration. Then a graph was plotted between concentration and response ratio (Chauhan *et al.*, 2015).

Accuracy

The accuracy of the proposed methods was assessed by recovery studies at three different levels i.e. 80%, 100%, 120%. The recovery studies were carried out by adding known amount of standard solution of AGT and PGZ to preanalysed tablet solutions. The resulting solutions were then re-analysed by proposed methods. Whole analysis procedure was repeated to find out the recovery of the added drug sample. This recovery analysis was repeated at 3 replicate of 5 concentrations levels (Ravisankar *et al.*, 2014).

Precision

Precision of the methods was studied at three level as at repeatability, intermediate precision (Day to Day and analyst to analyst) and reproducibility (Srivastava and Kumar, 2017). Repeatability was performed by analyzing same concentration of drugs for five times. Day to Day was performed by analyzing 5 different concentration of the

drug for three days in a week. The results are shown in tables.

Analysis of tablet sample

Twenty marketed tablets of AGT and PGZ were weighed and ground to a fine powder; amount equal to 25mg of AGT was taken in 10 ml volumetric flask. The PGZ present in this amount of tablet powder was 30mg. Then 8 ml of 2M Ammonium Acetate: 2M Sod. Citrate (1:1) solution was added and the flask was sonicated for about 10 min to solubilize the drug present in tablet powder and the volume was made up to the mark with hydrotropic solution. After sonication filtration was done through Whatman filter paper No. 41. Filtrate was collected and further diluted with Water to get the final concentrations of both drugs in the working range. The absorbances of final dilutions were observed at selected wavelengths and the concentrations were obtained from simultaneous equation method. The procedure was repeated for five times (Devi *et al.*, 2013; Daksh *et al.*, 2015).

RESULTS AND DISCUSSION

The UV spectrophotometric method developed for the simultaneous estimation of Alogliptin (AGT) and Pioglitazone (PGZ) using the hydrotropic phenomenon demonstrated excellent linearity, accuracy, and precision, confirming its suitability for routine analysis of these drugs in combined dosage forms.

The linearity study (Table 1) showed a direct relationship between absorbance and concentration over the range of 5–25 µg/ml for both AGT and PGZ. The regression coefficients (R^2) were found to be **0**.9997 for AGT and 0.9998 for PGZ, indicating excellent linearity. The %RSD values for both drugs were within 0.099–0.411 for AGT and 0.133–1.152 for PGZ**,** which are well within the acceptable limit of ≤2%, signifying the reliability of the method in the specified concentration range.

The accuracy of the method was evaluated by recovery studies at three levels (80%, 100%, and 120%). The recovery results (Table 2) were close to 100% for both AGT (98.24–98.85%) and PGZ (97.64–98.51%), confirming the accuracy of the method. The precision study, including repeatability, day-to-day, and analyst-to-analyst variations, showed %RSD values below 2% for both drugs, which demonstrates the precision and reproducibility of the method.

The assay results for the marketed tablet formulation (Table 3) revealed that the amount of AGT and PGZ found was 24.85 mg (99.40%) and 29.75 mg (99.17%)**,** respectively, which is within the permissible limits (±5% of the label claim) as per ICH guidelines. The low %RSD (≤0.225) further confirms the reliability of the method for routine quality control.

The results collectively confirm that the developed UV spectrophotometric method based on the hydrotropic phenomenon is simple, accurate, precise, reproducible, and cost-effective. It can be successfully applied for the simultaneous determination of Alogliptin and Pioglitazone in bulk and pharmaceutical formulations, making it a suitable alternative to more expensive chromatographic techniques.

Table 1: Linearity Data of Alogliptin and Pioglitazone

Drug	Linearity (µg/ml)	λ_{max}	Mean ± SD	%RSD	Slope	Intercept	Regression Coefficient
Alogliptin	5–25	276nm	0.278 ± 0.001 – 1.425 ± 0.002	0.099 – 0.411	0.0567	0.006	0.9997
Pioglitazone	5–25	224nm	0.113 ± 0.001 – 0.530 ± 0.001	0.133 – 1.152	0.0211	0.0027	0.9998

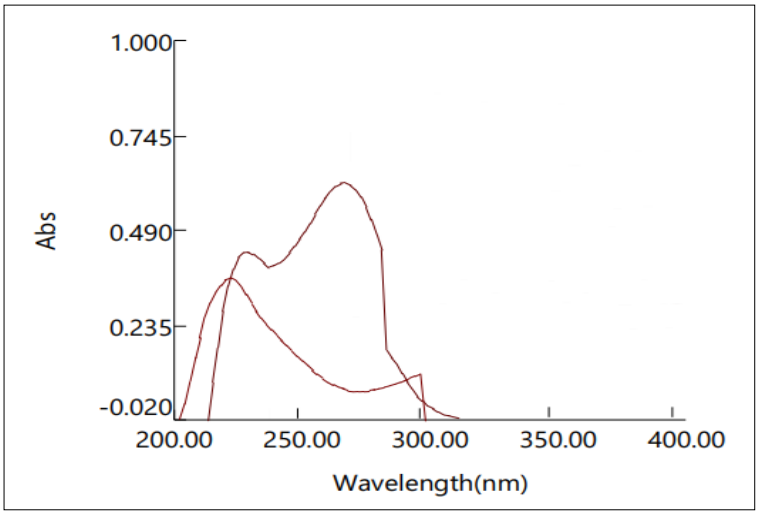

Figure 1: Overlain Spectra of both drug

Table 2: Summary of validation parameters for AGT and PGZ

Parameter	AGT			PGZ		
	Mean %	SD	%RSD	Mean %	SD	%RSD
Recovery (80%)	98.850	0.360	0.360	97.640	0.994	1.019
Recovery (100%)	98.420	0.862	0.876	98.100	0.835	0.852
Recovery (120%)	98.240	0.708	0.720	98.510	1.062	1.078
Repeatability	98.144	0.116	0.118	98.269	0.124	0.127
Day-to-Day Variation	98.512	0.150	0.153	98.541	0.101	0.102
Analyst-to-Analyst	98.299	0.134	0.137	99.020	0.061	0.061
Reproducibility	98.349	0.112	0.114	98.219	0.103	0.104

Table 3: Analysis of tablet formulation of AGT and PGZ

Drug	Label claim (mg)	Amount found (mg)	Label claim (%)	S.D.	% RSD
AGT	25	24.85	99.40	0.115	0.116
PGZ	30	29.75	99.17	0.223	0.225

CONCLUSION

The present study successfully developed and validated a simple, rapid, and cost-effective UV spectrophotometric method for the simultaneous estimation of Alogliptin (AGT) and Pioglitazone (PGZ) using the hydrotropic phenomenon. The method exhibited excellent linearity over the range of 5–25 µg/ml**,** with high regression coefficients ($R^2 > 0.999$), confirming its reliability. Recovery studies indicated good accuracy, while precision parameters such as repeatability, day-to-day, and analyst-to-analyst variations showed %RSD values well within the ICH acceptance criteria (<2%), demonstrating reproducibility and robustness. The assay of the marketed tablet formulation revealed drug content within 99–100% of the label claim**,** confirming the suitability of the method for routine quality control analysis. This method offers a green, economical, and accurate alternative to chromatographic techniques and can be effectively applied for regular analysis of Alogliptin and Pioglitazone in bulk drug and pharmaceutical dosage forms.

DECLARATION OF INTEREST

The authors declare no conflicts of interests. The authors alone are responsible for the content and writing of this article.

REFERENCES

- Chaudhari, R. Y., Patel, S. A., & Desai, S. D. (2015). Development and validation of RP-HPLC method for simultaneous estimation of alogliptin and pioglitazone in tablet dosage form. *International Journal of Pharmacy and Pharmaceutical Sciences, 7*(3), 357–361.
- Crammer, J. L., & Hunter, J. E. (1982). Hydrotropic solubilization. *Chemical Society Reviews, 11*(1), 1–21.
- International Conference on Harmonisation. (2005). *ICH harmonised tripartite guideline: Validation of analytical procedures: Text and methodology Q2(R1).* ICH.
- Mahaparale, S. P., Dharmadhikari, V. S., & Chandewar, A. V. (2020). Simultaneous UV-spectrophotometric estimation of alogliptin and pioglitazone in bulk and combined dosage form. *Journal of Pharmaceutical Research International, 32*(13), 33–40.
- Maheshwari, R. K., Chaturvedi, S. C., & Jain, N. K. (2006). Novel application of hydrotropic solubilization in spectrophotometric analysis of poorly water-soluble drug. *Indian Journal of Pharmaceutical Sciences, 68*(2), 195–198.
- Nakahara, T., Takeuchi, M., Hongu, M., et al. (2011). Effects of alogliptin, a DPP-4 inhibitor, in patients with type 2 diabetes mellitus. *Endocrine Journal, 58*(10), 869–876.
- Rajput, S. J., & Raj, H. A. (2011). Application of mixed hydrotropic solubilization technique in spectrophotometric analysis of poorly water-soluble drug. *Indian Journal of Pharmaceutical Sciences, 73*(6), 682–685.
- Sharma, M. C., Sharma, S., & Kohli, D. V. (2018). Simultaneous estimation of alogliptin and pioglitazone by RP-HPLC in pharmaceutical formulation. *Asian Journal of Pharmaceutical and Clinical Research, 11*(4), 331–335.

- Soccio, R. E., Chen, E. R., & Lazar, M. A. (2014). Thiazolidinediones and the promise of insulin sensitization in type 2 diabetes. *Cell Metabolism, 20*(4), 573–591.
- Rane, J., Thakre, V., Bakal, R. L., & Patil, S. (2015). Novel spectrophotometric estimation of gliclazide by using mixed hydrotropic solubilization phenomenon. *Journal of Drug Discovery and Therapeutics, 3*(27), 8–10.
- Khan, M. A. (2015). Enhancement of solubility of poorly water soluble drugs Diclofenac sodium by mixed solvency approach. *International Journal of Research and Development in Pharmacy and Life Sciences, 4*(6), 1835–1837.
- Chauhan, A., Mittu, B., & Chauhan, P. (2015). Analytical method development and validation: A concise review. *Journal of Analytical & Bioanalytical Techniques, 6*(1), 1–5.
- Ravisankar, P., Gowthami, S., & Rao, G. D. (2014). A review on analytical method development. *Indian Journal of Research in Pharmacy and Biotechnology, 2*(3), 1183.
- Srivastava, R. K., & Kumar, S. S. (2017). An updated review: Analytical method validation. *European Journal of Pharmaceutical and Medical Research, 4*(1), 774–784.
- Devi, T. P., Setti, A., Srikanth, S., Nallapeta, S., Pawar, S. C., Rao, J. V., et al. (2013). Method development and validation of paracetamol drug by RP-HPLC. *Journal of Medical and Allied Sciences, 3*(1), 8.
- Daksh, S., Goyal, A., & Pandiya, C. K. (2015). Validation of analytical methods: Strategy and significance. *International Journal of Research and Development in Pharmacy and Life Sciences, 4*(1), 1489–1497.