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DEVELOPMENT AND VALIDATION OF DERIVATIVE SPECTROPHOTOMETRIC METHOD FOR ESTIMATION OF PIMOZIDE

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ABSTRACT

***Objective**: The objective of the present research work was to develop and validate derivative spectrophotometric method for estimation of Pimozide from the bulk and tablet dosage form. **Methods:** The stock solution of Pimozide was prepared in methanol and further dilution was done in 0.1 N HCl. λ_{max} of Pimozide was found at 278 nm. This work proposes second order derivative method for determination of Pimozide by measuring amplitude at 271.60 nm using Δλ 2 and scaling factor 10. The content of Pimozide was determined by using regression equation. **Results**: The method was found linear in the concentration range of 5-70 µg/ml. The mean % assay was found as 100.95% and % recovery of Pimozide was found in the range of 99.12-101.14%. The % R.S.D. for Intraday, Interday precision and Repeatability study was observed less than 2%. **Conclusion:** The developed method was found to be simple, economic, specific, accurate and precise which can be adopted in pharmaceutical industry.*

***Key Words:** Pimozide, Derivative Spectrophotometric Method, Validation.*

INTRODUCTION

Pimozide (PIMO) is an antipsychotic drug used in Schizophrenia and Tourette syndrome. Chemically it is 1-[1-[4,4-Bis(4-fluorophenyl)butyl]piperidin-4-yl]-1,3-dihydro-2H-benzimidazol-2-one [1]. Pimozide helps to ease the symptoms of Schizophrenia. It is also used to reduce uncontrolled movements (motor tics) or outbursts of words/sounds (vocal tics) caused by Tourette syndrome. It is a medication that works by decreasing the activity of dopamine in the brain [2]. Chemical structure of PIMO is shown in Fig. 1.

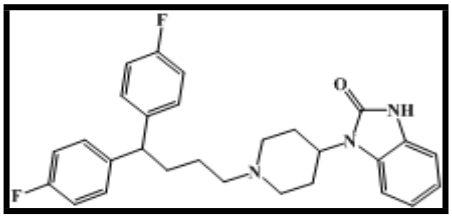

Fig. 1: Chemical Structure of Pimozide

OBJECTIVE

Literature survey revealed that few analytical methods are reported for estimation of PIMO like HPLC using fluorescence detection [3], Colorimetric method [4], Differential Pulse Voltametric method [5], LC/MS method [6], Stability indicating HPTLC method [7] and Spectrophotometric methods [8,9,10]. It was observed that, none of the derivative UV Spectrophotometric method is reported for the quantification of the PIMO in tablet dosage form. Hence in present research work attempt has been made for development and validation of UV Spectrophotometric method for estimation of PIMO in tablet dosage form.

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MATERIAL AND METHODS

Instrument:

A Shimadzu UV- Visible double beam spectrophotometer model 1700 (Japan) with 1cm matched quartz cells connected to a computer running UV- Probe 2.32 software for absorbance measurements and treatment of data was used along with Sartorius digital balance for weighing.

Chemicals and Reagents:

PIMO working standard powder was kindly provided by Micro Lab Ltd, Bangalore. Pimozide tablets (Mozep-2, Intas Pharmaceutical Ltd) containing 2 mg of PIMO were purchased from local pharmacy.

Selection of Solvent:

To select suitable solvent, solutions of PIMO was prepared separately in methanol and 0.1N HCl (stock solution in methanol). These solutions were scanned in the UV region (200-400 nm) and the spectra were studied for intensity of absorbance and wavelength of absorbance.

Calibration Curve for PIMO:

For construction of calibration curve, the solutions of PIMO in the concentration range 5-70 µg/ml were prepared in 0.1 N HCl and scanned in the UV region from 200 to 400 nm. These spectra were transformed into second order derivative, using UV Probe software at Δλ 2 and scaling factor 10. The amplitude of the corresponding troughs was measured at 271.60 nm and calibration curve was plotted. Second order derivative overlay spectra of PIMO are shown in figure 2.

Analysis of Marketed Formulation:

Twenty Tablets of PIMO (Mozep-2) were weighed accurately and finely powdered. The powder equivalent to 10 mg of PIMO was transferred to 100 ml volumetric flask. The drug was extracted using ultasonication for 15 min in about 50 ml of AR grade methanol. The volume was made upto the mark using same solvent to get concentration of 100 µg/ml of PIMO. The resulting solution was filtered through whatman filter paper no 41. From the above solution 3 ml of aliquot was transferred to 10 ml volumetric flask and the volume was made upto the mark with 0.1 N HCl to get

concentration of 30 µg/ml of Pimozide. The solution was scanned in the UV region. The spectrum was transformed into second order derivative (Δλ 2, scaling factor 10) and amplitude of the trough was recorded at 271.60 nm. The concentration of PIMO was calculated from linear regression equation. Results of estimation of PIMO are shown in Table 1.

Method Validation:

The proposed method of analysis of PIMO was validated as per the recommendations of ICH guidelines for the parameters like accuracy, linearity, precision, detection limit and quantitation limit.

To study the accuracy of the proposed method, recovery studies were carried out by standard addition method at three different levels (80%, 100% and 120%) of assay concentration. A known amount of standard PIMO was added to preanalysed tablet powder and percent recoveries were calculated.

The precision of the method was determined by performing intermediate precision (intraday, interday and variation by different analyst) and repeatability study (n=6) and was expressed as % Relative Standard Deviation (% RSD). Intraday precision was determined by performing nine determinations from triplicate injections of three different concentrations of PIMO (10, 30, 50 µg/ml) on the same day at different time intervals and on three different days for interday precision. Variation of results by different analyst was checked by performing assay in triplicate by Analyst I and Analyst II and comparing their results by F- test and t-Test.

Sensitivity of the method was determined by means of the detection limits (LOD) and quantification limit (LOQ). Calculations for LOD and LOQ were based on ratio of standard deviation of y-intercept of the calibration curves (σ) and average slope of the curve (S), using the equation LOD=3.3 x σ/S and LOQ=10 x σ/S.

RESULTS AND DISCUSSION

Considering the solubility of PIMO the stock solution was prepared in methanol and further dilution was done in methanol and 0.1 N HCl. As PIMO showed maximum absorbance in 0.1 N HCl, it was selected as solvent for further dilutions.

The excipients in the marketed formulation were showing prominent absorbance at λ_{max} of the drug in zero order spectrophotometric method. Hence, it was thought to develop second order derivative method for estimation of PIMO.

The method showed linearity in the concentration range of 5-70 µg/ml. The mean % assay was found as 100.95% while, results of recovery studies were found in the range of 99.12-101.14%. LOD and LOQ of PIMO were found to be 0.546 µg/ml and 1.656 µg/ml, respectively. The % R.S.D. for Intraday, Interday precision and Repeatability study was observed less than 2%.

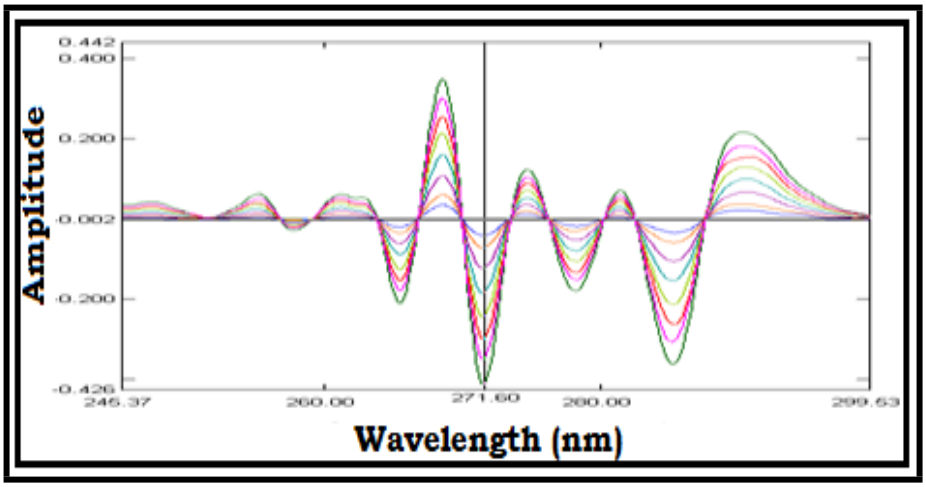

Fig. 2: Overlay of Second Order Derivative Spectra of PIMO

Table No. 1: Results of PIMO Estimation

Sr.No.	Parameters	Results of PIMO
1	Linearity (µg/ml)	5 to 70
2	Y=mx+c	Y = -0.0058x-0.0082
3	Correlation coefficient (r^2)	0.9992
4	%Assay (Mozep-2)	100.95%
5	% Recovery	99.12- 101.14 %
6	LOD (µg/ml)	0.546
7	LOQ (µg/ml)	1.656

CONCLUSION

It can be concluded that the developed second order spectrophotometric method for estimation of Pimozide in tablet dosage form is simple, economical, accurate and reproducible and will be conveniently adopted for the routine quality control analysis from its pharmaceutical formulations and bulk drug.

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