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# A NOVEL VALIDATED RP-HPLC METHOD FOR ESTIMATION OFPROPIOMAZINE IN BULK AND PHARMACEUTICAL DOSAGE FORMS

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## ABSTRACT

A simple, rapid, accurate, precise and reproducible RP-HPLC method was developed for the estimation of Propiomazine in liquid dosage forms. The method was carried out using Inertsil ODS 3V(150mm x 4.6 mm), 5µm column in an binary mode with mobile phase comprising gradient mixture of pH 3.0 Potassium Di-Hydrogen phosphate and Acetonitrile. The flow rate was 1.2 ml/min and detection was carried out at 260 nm using a UV detector. The retention time for Propiomazine was found to be at 3.76 min and 9.74 min. The method for Propiomazine showed linearity in the concentration range of 153.7- 461µg/ml ($R^2$=1.000) and for Propiomazine showed linearity in the concentration range of 12.6-37.8µg/ml ($r^2$=0.9997). The recovery studies for Propiomazine also carried out and %RSD for reproducibility was found to be below 2%. The method was simple, sensitive and specific. Hence method can be used for the quantification of Propiomazine in pharmaceutical dosage form.

**Key Words**: Propiomazine; RP-HPLC; ICH validation; PDA Detector.

## Introduction

**Propiomazine** is a member of the class of phenothiazines that is 10H-phenothiazine substituted by a 2-(dimethylamino)propyl group at nitrogen atom and a propanoyl group at position 2.It is a member of phenothiazines, an aromatic ketone and a tertiary amino compound. It derives from a hydride of a 10H-phenothiazine.

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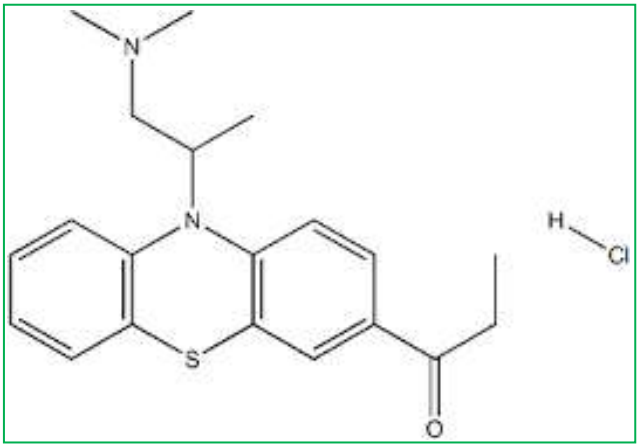


**Fig.01.Chemical Structure of Propiomazine.**

Propiomazine, an atypical antipsychotic agent, is used to treat both negative and positive symptoms of schizophrenia, acute mania with bipolar disorder, agitation, and psychotic symptoms in dementia. Future uses may include the treatment of obsessive-compulsive disorder and severe behavioral disorders in autism. Structurally and pharmacologically similar to clozapine, propiomazine binds to alpha(1), dopamine, histamine H1, muscarinic, and serotonin type 2 (5-HT2) receptors.

**Mechanism of action**

Propiomazine acts as an antagonist of dopamine 1, 2, and 4 receptors, serotonin (5-HT) receptor types 2A and 2C, muscarinic receptors 1 through 5, alpha(1)-receptors, and histamine H1-receptors. Its main use as a sedative is due to its antihistamine effect.

**Method Development and optimization of Propiomazine**:

**Preparation of solutions:**

**Diluent:** Based up on the solubility of the drug diluent was selected, Methanol taken in the ratioof 50:50.

**Preparation of standard stock solutions:** Accurately weighed 10mg of Propiomazine transferred in 10ml volumetric flask 3/4$^{th}$ of diluent was added and sonicated for 10 mins. Flask was made up with diluent and labelled as standard stock solution (1000ug/ml).

**Preparation of standard working solution:** One ml of Propiomazine from stock solution was pipette out and taken into a 10ml volumetric flask and make up with diluents (100ug/ml).

**Determination of wavelength:**

Standard working solution was scanned between 200-400nm in double beam UV-Visible spectrophotometer. Maximum absorbance ($\lambda_{max}$) for the Propiomazine was determined by UV spectrophotometer and observed that maximum absorbance at 247nm.

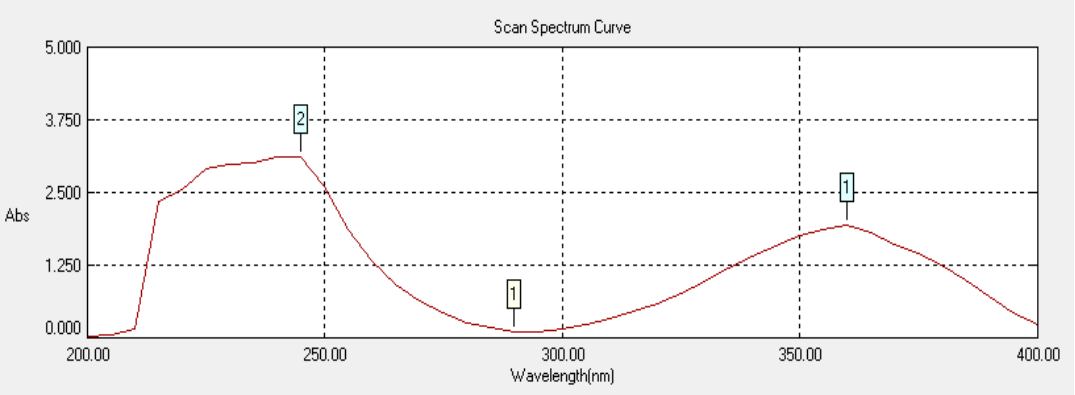


**Fig.2 Propiomazine UV-Visible Spectrum**

**Chromatographic condition:**

**Stationary Phase** : INERTSIL ODS 3V (5um 4.6×250nm)

**Wavelength** : 247nm

**Flow rate** : 1.0ml/min

**Temperature** : $30^0$C
**Injection volume** **:** 20ul
**Run time** : 5 min
**Mobile phase** : Acetonitrile: water (80:20)

**Diluent** **:** Methanol :Water

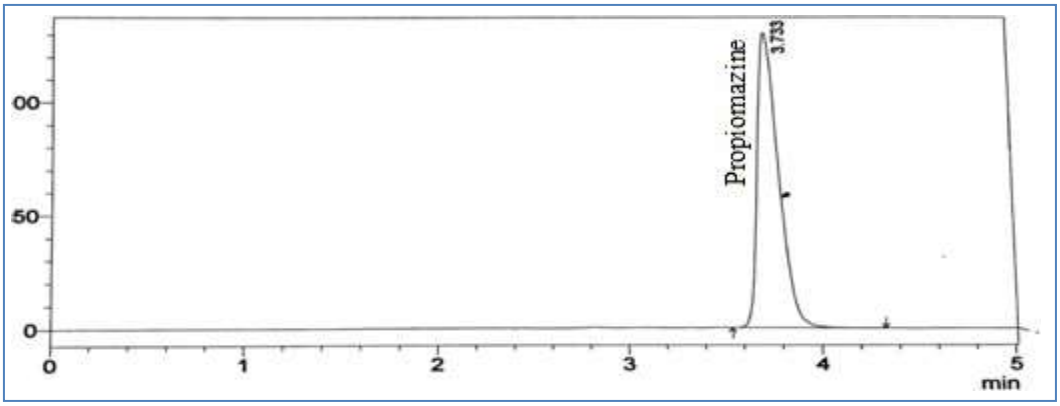


**Fig.3 Typical Chromatogram of Propiomazine**

## RESULTS AND DISSCUSSION

### Method validation:

**Linearity:** The concentration range of 10-50 µg/ml for Propiomazine and all the standard solutions were filtered and injected.

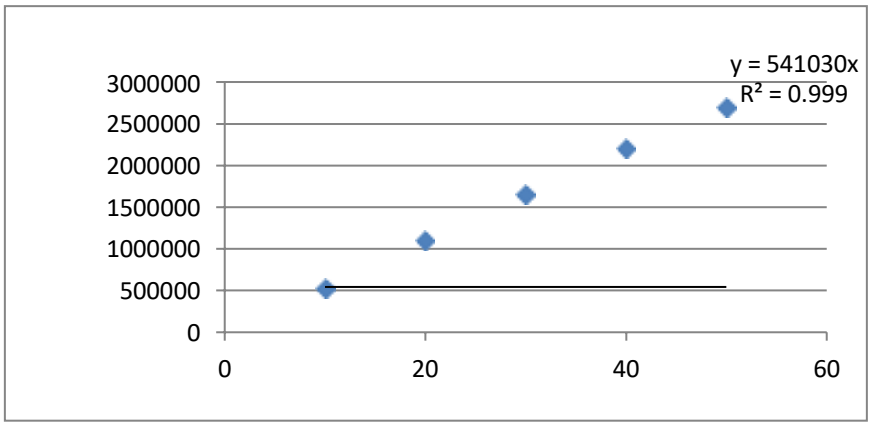


**Fig.03 Calibration curve of Propiozamine**

**Table 1 Linearity data of Propiomazine**

| Linearity level | Concentration (µg/ml) | Peak Area | | Mean |
|---|---|---|---|---|
| | | Set 1 | Set 2 | |
| 1 | 10 | 531665 | 533356 | 531088 |
| 2 | 20 | 1106624 | 1106424 | 1106524 |
| 3 | 30 | 1650303 | 1652426 | 1651364 |

| | | | | |
|---|---|---|---|---|
| 4 | 40 | 2201066 | 2201266 | 2201166 |
| 5 | 50 | 2693870 | 2683944 | 2688907 |

**Table: 2 Precision data of Propiomazine**

| S.NO | Concentration (µg/ml) | Amount (µg/ml) | % of Amount | Avg | S.D | %RSD |
|---|---|---|---|---|---|---|
| 1 | 30 | 30.1 | 100.3 | 100.2 | 0.90 | 0.89 |
| 2 | | 30.1 | 100.3 | | | |
| 3 | | 30 | 100 | | | |
| 4 | | 30.1 | 100.3 | | | |
| 5 | | 30.1 | 100.3 | | | |
| 6 | | 30 | 100 | | | |

**Accuracy**

Accuracy was done by recovery studies

**Accuracy:** Three concentrations of 50%, 100% and 150% are prepared and injected.

**Preparation of 50% Spiked solution:** 3.0ml of sample stock solution was taken into a 10ml volumetric flask, to that 1.5ml from each standard solution was pipette out and make up the markwith diluents.

**Preparation of 100% Spiked solution:** 3.0ml of sample stock solution was taken into a 10ml volumetric flask, to that 3.0ml from each standard solution was pipette out and make up the markwith diluents.

**Preparation of 150% Spiked solution:** 3.0ml of sample stock solution was taken into a 10ml volumetric flask, to that 4.5ml from each standard solution was pipette out and make up the markwith diluents.

**Table 3 Accuracy data**

| Percentage level | Amount (µg/ml) | Amount added (µg/ml) | Amount found | Amount Recovery | % Recovery | Avg % | S.D | %RSD |
|---|---|---|---|---|---|---|---|---|
| 50 | 30 | 15 | 44.9 | 14.9 | 99.3 | 100.6 | 1.1 | 1.09 |
| | | | 45.2 | 15.2 | 101.3 | | | |
| | | | 45.2 | 15.2 | 101.3 | | | |
| 100 | | 30 | 60.1 | 30.1 | 100.3 | 100.7 | 0.40 | 0.41 |
| | | | 60.3 | 30.3 | 101 | | | |
| | | | 60.3 | 30.3 | 101 | | | |
| 150 | | 45 | 74.8 | 44.8 | 99.5 | 99 | 0.93 | 0.93 |
| | | | 74.1 | 44.1 | 98 | | | |
| | | | 74.9 | 44.9 | 99.7 | | | |

**Limit of detection & Limit of quantification:**

The limit of detection and the limit of quantification were calculated by using the average value of slope and the standard deviation of intercept and the results are listed in the table.4

**Table 4.Data of LOD and LOQ**

| SNO | Parameters | Propiomazine |
|---|---|---|
| 1 | LOD | 0.15 |
| 2 | LOQ | 0.48 |

**Robustness:**

Robustness was done by changing the column temperature (±5$^0$C), flow rate (±10$^O$C), changing the wavelength (± 5nm), and organic compounds of mobile phase (±5%). All the system suitability parameters must be met as per the method.

1. The tailing factor of Propiomazine maleate should be not more than 2 for variation in flow and wavelength.

2. The % RSD of asymmetry and retention time for fexofendine should be not more than 2%for variation in flow and wavelength.Small deliberate change in the method is made like Flow minus, Flow plus, Wavelength minus, Wavelength plus, Temperature minus, Temperature plus. The % RSD of the above conditions is calculated shown Table 5.

**Table 5 Robustness studies of Propiomazine maleate**

| Parameter | Conditions | Variation | %RSD |
|---|---|---|---|
| Wavelength Variation | 245 | 250 | 2 |
| | | 240 | 0.55 |
| Column oven temperature Variation | 30°c | 25°c | 1.3 |
| | | 35°c | 0.95 |
| Flow rate Variation | 1ml/min | 0.9ml/min | 0.22 |
| | | 1.1ml/min | 0.39 |

## 7. SUMMARY AND CONCLUSION

Propiomazine was determined by RP-HPLC method, optimisation of chromatographic parameters was done. Parameters were optimised by altering the mobile phase ratio and flow rate at a wavelength of 247 nm. The trails for optimisation were conducted by using different mobile phases which include Acetonitrile: Watere (90:10), ACN: Water (80:20), Methanol: Water (90:10), ACN: Water (75:25). Out of all trails, 75:25 ratio of ACN: Water (80:20) at 0.7ml/min flow rate was selected for this proposed method and its shows good system suitability values which include, tailing factor, retention time, no. of theoretical plates.The calibration was performed by using external calibration method. The stock solution of Propiomazine was prepared and dilution was made by using mobile phase and absorbance was measured at 247 nm. Serial dilutions 10 to 50 µg/ml of Propiomazine were prepared and injected and the chromatograms are recorded. The calibration curve using peak area Vs concentration was plotted. The correlation co efficient was calculated as 0.999, the system precision was done both intraday and interday and the % RSD is below 2.

The recovery studies were passed out to confirm the accuracy of the method by added standard drug to a previously analysed formulation. The average percentage recovery was appeared as 101%. LOD and LOQ were calculated and were in within limits.Robustness was performed by deliberate changes in the optimised condition such as flow rate, temperature, wave length, and chromatograms were noted.Twenty tablets are accurately weighed; powdered and

equivalent quantity i.e. 50 mg of Propiomazine tablet powder was taken and diluted by using diluent. The percentage of Propiomazine present in the formulation was occurred to be 101%.

Here by concluded that the method showed tremendous sensitivity, reproducibility, accuracy and repeatability, which is proved the low percentage relative standard deviation. The results of recovery studies, determines that there is no interference from the excipients used in formulation. RP-HPLC method can be effectively applied for the routine analysis of Propiomazine pure and tablet formulation in quality control analysis.

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