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Stability Indicating Chromatographic Method Development And Validation for The Simultaneous Estimation of Ilaprazole And Domperidone in its Pharmaceutical Dosage Form By Hplc

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ABSTRACT

A specific, accurate, precise and reproducible RP HPLC method has been developed and subsequently validated for the simultaneous estimation of Ilaprazole and Domperidone in pharmaceutical dosage form. The proposed HPLC method utilizes hypersil (Thermo scientific) C18 column (250 mm × 4.6 mm id, 5 µm particle size), and mobile phase consisting of water:Acetonitrile:Acetic acid (30:70:0.1) at a flow rate of 1.0 mL/min. This method has been successively applied to marketed formulation and no interference from the formulation excipients was found.

KEYWORDS | Ilaprazole, Domperidone, Stability indicating assay, HPLC

1.INTRODUCTION

For the development of stability-indicating assay method, the drug is subjected to Various ICH (International Conference on Harmonization) stress conditions such as photolytic, hydrolytic, thermal and oxidative. As per the ICH drug stability test guidelines Q1A (R2), validated stability-indicating assay method should be developed for the analysis of drug substance and drug product. Ilaprazole; 2-[[(4-Methoxy-3-methyl-2-pyridinyl) methyl]sulfinyl]-6-(1Hpyrrol-1-yl)-1H-benzimidazole is a new proton pump inhibitor used in the treatment of pepticulcer disease, dyspepsia, gastro esophageal reflux disease and duodenal ulcer which reduces acid secretion by inhibiting the parietal cell H+/K+ ATP pumpDomperidone **(DOM),** chemically is known as 5-chloro-1-{1-[3-(2-oxo-2,3-dihydro-1H-1,3-benzodiazol-1-yl)propyl]piperidin-4-yl}-2,3-dihydro-1H-1,3-benzodiazol-2-one, a specific blocker of dopamine receptors. The aim of the present study was to develop and validate stability-indicating HPLC method for determination of Ilaprazole (IPZ) and Domperidone bulk drug as per the ICH guideline. The developed method is stability-indicating and was successfully utilized for the determination of Ilaprazole in tablet formulation.

2. MATERIALS AND METHODS

2.1 Apparatus and Instrument The analysis was carried out on a HPLC system (WATERS Milford USA) equipped with PDA detector. Other apparatus and instruments used were a micro analytical balance (Shimadzu), Ultrasonic Cleaner (EIE Instruments Pvt. Ltd. Ahmedabad), Nylon Membrane Filters (0.22mcm, 47 mm D). All instruments and glass wares were calibrated.

2.2 Reagents and Materials Ilaprazole and Domperidone were obtained as gratis sample from Accurate Pharmaceuticals, Godhra. Methanol HPLC Grade, Water HPLC Grade, A stock-standard solution of ILA and DOM was prepared by dissolving accurately weighed amount of pure drug in mobile phase.

2.3 Mobile Phase: . The mobile phase water:Acetonitrile:Acetic acid (30:70:0.1) was filtered through Millipore filter paper type HV (0.45 µm) and degassed by sonication.

2.4 Chromatographic conditions Chromatographic analysis was carried out on an hypersil C-18 column, (5 µm, 250mm x 4.6mm i.d) LC-20 AT. The mobile phase consisted of water:Acetonitrile:Acetic acid (30:70:0.1). The mobile phase was filtered through Millipore filter paper type HV (0.45 µm) and degassed by sonication, was pumped at 1.0 ml/min flow rate. The column was thermostated at room temperature. Under these conditions the runtime was 10 min.

2.4.1 Preparation of standard stock solution of Ilaprazole (100 µg/ml) and Domperidone (300µg/ml) A 10 mg of standard Ilaprazole and 30 mg of standard Domperidone was weighed and transferred to a 100 ml volumetric flask each and dissolved in 25 ml mobile phase. The flask was shaken and volume was made up to the mark with mobile phase to give a solution containing 100 µg/ml Ilaprazole and 300 µg/ml Domperidone

2.4.2 Preparation of combined working standard solution containing Ilaprazole and Domperidone in ratio of 1:3
Accurately weighed 10 mg Ilaprazole and 30 mg of Domperidone were transferred to 100 ml volumetric flask, dissolved in sufficient amount of mobile phase and diluted up to mark with mobile phase to get concentration of 100 µg/ml Ilaprazole and 300 µg/ml Domperidone. This solution was diluted further to get the concentrations in range of 5, 7.5, 10, 12.5, 15 µg/ml of Ilaprazole and 15, 22.5, 30, 37.5, 45 µg/ml of Domperidone.

2.5 Degradation Studies:
All stress studies for Ilaprazole and Domperidone were performed at concentration of 1mg/ml. The neutral (water) degradation study was performed by refluxing the drug solution at 800C for 8h. The alkaline degradation study was carried out by refluxing drug solution in 0.1N NaOHat 80C for 4h. The drug solution was refluxed with 0.1N HCl at 80C for 4h to conduct degradation study under acidic conditions. For degradation study in hydrogen peroxide (H2O2) drug solution was refluxed with 3% H2O2 at 80C for 8h. Photolytic stress degradation study was carried out by exposing the drug powder to UV light for 48h. Thermal degradation behavior of Ilaprazole and domperidone was studied by exposing the drug powder to dry heat in an oven at 80C for 24h. samples were withdrawn periodically and analyzed by HPLC after suitable dilution.

3.RESULTS AND DISCUSSION

The HPLC isocratic programming was utilized to analyze drug and its degradation products. The separation was achieved with mobile phase consisting of water: methanol initially in ratio 50:50 but no peak were observed so mobile phase water:Acetonitrile (30:70) was tried and Ilaprazole peak single was observed. Then again using isocratic conditions water:Acetonitrile:acetic acid were carried out. After considering the varying combinations of various mobile phases, Water: Acetonitrile: Acetic acid (30:70:0.1) was finalized as it was showing good peak shapes and a significant amount of resolution.

The Chromatograms of Ilaprazole and Domperidone standards

and Ilaprazole and Domperidone sample show no interference with the Chromatogram of Ilaprazole and Domperidone Blank, so the Developed method is Specific.

The linearity for Domperidone and Ilaprazole were assessed by analysis of combined standard solution in range of 15-45 µg/ml and 5-15 µg/ml respectively. The % RSD for Ilaprazole and Domperidone was found to be 0.704 and 0.747 respectively. The % R.S.D. for Intraday precision was found to be 0.259-0.950. for Domperidone and 0.202-0.861 for Ilaprazole. The % R.S.D. for interday precision was found to be 0.893-1.753 for Domperidone and 0.706-1.055 for Ilaprazole.

Accuracy of the method was confirmed by recovery study from marketed formulation at three level of standard addition. Percentage recovery for Domperidone was 100.900-101.458 %, while for Ilaprazole, it was found to be in range of 100.365-100.837 %.

Applicability of the proposed method was tested by analyzing the commercially available Capsule formulation Lupila-D .

The assay results were comparable to labeled value of each drug in Capsule dosage form. These results indicate that the developed method is accurate, precise, simple and rapid. It can be used in the routine quality control of dosage form in industries.

CONCLUSION

The stability-indicating assay has been developed and validated for the determination of Ilaprazole and Domperidone in bulk drug and tablet dosage form. The degradation behavior of Ilaprazole and Domperidone was studied as per ICH recommended conditions. The proposed method is simple, precise, accurate, specific, and is able to separate drug from its degradation products. The developed method could also be extended to the analysis of stressed marketed formulation of Ilaprazole and Domperidone, as there is no interference from excipients or other components observed.