JOURNAL OF PHARMACEUTICAL SCIENCE AND BIOSCIENTIFIC RESEARCH (JPSBR)

(An International Peer Reviewed Pharmaceutical Journal that Encourages Innovation and Creativities)

Absorption Correction Method for Simultaneous Estimation Domperidone and Ilaprazole by UV Spectrometry

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ABSTRACT:

Domperidone and Ilaprazole are drugs used in the treatment of gastro-oesophageal reflux. They are also given in combination. The current work describes a simple UV spectrophotometric method for estimation of these two in combination. It is based on the principle of Absorbance correction for interference. The choice of 285nm and 320 nm is based on the fact that Ilaprazole shows practically negligible absorbance at 320 nm whereas both these drugs absorb significantly at 285 nm. The method is economical, fast and has been checked for linearity, accuracy, precision, LOD, and LOQ.

KEY WORDS: Domperidone, Ilaprazole, Absorbance corrected method, Validation.

INTRODUCTION:

Domperidone, a drug used in the treatment of gastro-oesophageal reflux disease, is chemically 5-Chloro-1-(1- [3-(2- oxo- 2,3- dihydro -1H –benzo d] imidazol -1-yl)propyl]piperidin-4-yl)-1H-benzo[d]imidazol-2(3H)-one[1]. It increases gastrointestinal peristalsis resulting in increase in transit of food through stomach. It is used in relieving nausea and vomiting. Its molecular formula is C$_{22}$H$_2$ClN$_5$O$_2$. Ilaprazole, a proton pump inhibitor (PPI) is used in the treatment of dyspepsia, peptic ulcer disease (PUD), gastro-oesophageal reflux disease (GORD/GERD) and duodenal ulcer. Ilaprazole[2] chemically is 2-[(RS)-[(4-methoxy-3-methylpyridin-2-yl)methyl]sulfinyl]-5-(1H-pyrrol-1-yl)-1H-benzimidazole. Its molecular formula is C$_{19}$H$_{18}$N$_4$O$_2$S.
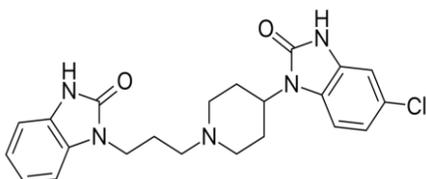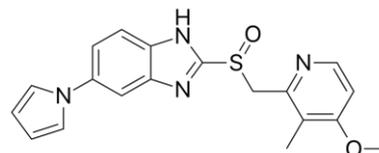

Figure 2 Structure of Ilaprazole

A thorough literature search revealed that there are number of HPLC methods[3-4], stability indicating chromatographic[5-9] and a UV spectro photometric [10] method reported for determination of Domperidone and Ilaprazole in combination. When UV spectrum of these two was overlapped, it was observed that Ilaprazole has considerable absorbance at 285 nm as well as 320 nm whereas Domperidone has appreciable absorbance at 285 nm but negligible absorbance at 320 nm. This suggests that absorbance correction method may be applicable to this combination[11].

MATERIALS AND METHODS
Apparatus:

Figure 1 Structure of Domperidone

Calibrated class A glassware, weighing balance of the make Shimadzu (model AY 120), JASCOV730 UV spectrometer, sonicator manufactured by Prama Solutions for Laboratory etc.

Reagents and materials:

Methanol AR, working standards of Domperidone &Ilaprazole, distilled water

Methodology:

Preparation of standard stock solution:

A calibrated class A volumetric flask of 25 ml was used for preparing the stock solutions of both the drugs. Weighing of individual Domperidone & Ilaprazole drugs was carried out using a weighing balance. 25mg of Ilaprazole was weighed, methanol was added and further proceeded to make up its volume up to 25ml. Thus Ilaprazole stock solution was prepared. 25mg of Domperidone was weighed, methanol was added and sonicated as the powdered drug Domperidone was slowly dissolvable, after sonication the volume was made up to 25ml resulting in Domperidone stock solution. These two stock solutions were diluted appropriately using distilled water.

Preparation of standardsolution:

ILAPRAZOLE

From the stock solution of Ilaprazole, appropriate volume was transferred to 10ml volumetric flasks and the volume was made up with distilled water to obtain concentrations in the range of 10-50 mcg/ml.

DOMPERIDONE:

Sample solutions of Domperidone was prepared in the similar manner as for Ilaprazole to obtain concentrations in the range of 25 to 75 mcg/ml.

RESULTS:

The spectrum of standard solutions was measured between 200 -400 nm.

It was observed that Domperidone has practically negligible absorbance at 320 nm whereas Ilaprazole absorbs at both 320 nm as well as 285 nm.
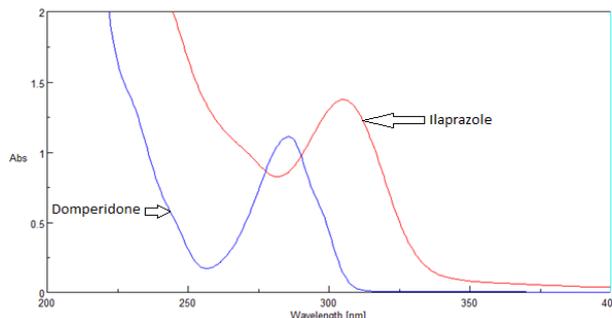

Figure 3 Overlay of Ilaprazole with Domperidone spectra.

PREPRATION OF SAMPLE:

Standard mixtures were prepared by diluting appropriate volume from each standard solution in one volumetric flask and diluting with distilled water.

Linearity (calibration curve):

The absorbance of each dilution of Ilaprazole was noted at 285nm and 320 nm. The absorbance of each dilution of Domperidone was measured at 285 nm. A linearity graph was plotted of the absorbance values obtained versus concentration of the drugs against the wavelength 285 and 320 nm. Here the concentration of the drug used were: Ilaprazole from the range of 10 to 50µg/ml and Domperidone from 25 to 75µg/ml
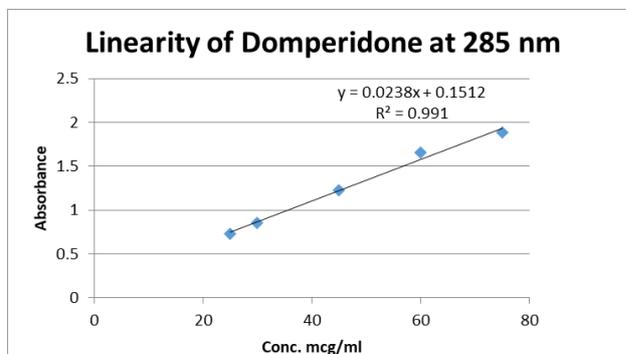

Figure 4 Linearity graph of Concentration in µg/ml versus Absorbance of Domperidone at 285nm

Similarly, for Ilaprazole, the linearity was checked.

At 320 nm, the linearity equation was y=0.029x-0.006 R2 0.980

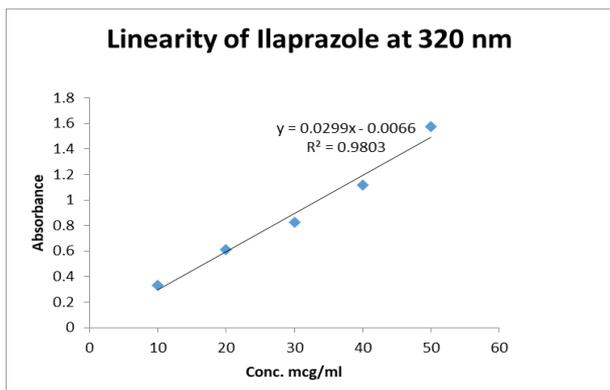At 285 nm, the linearity equation was y=0.028x+0.012 R2 0.964

Linearity of Ilaprazole at 320 nm

Figure 5 Linearity graph of Concentration in µg/ml versus Absorbance of Ilaprazole at 320nm

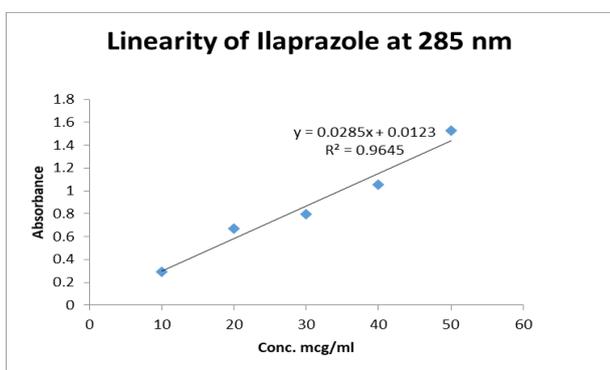## Linearity of Ilaprazole at 285 nm

Figure 6 Linearity graph of Concentration in µg/ml versus Absorbance of Ilaprazole at 285nm

Calibration curves for mixed combination of the drugs were prepared as mentioned above and their absorbance were measured against the wavelengths 285 and 320 nm respectively.

Assay of marketed capsules containing Domperidone and Ilaprazole was done by weighing an amount of capsule contents, dispersing in methanol, filtration through Whatman paper, followed by appropriate dilution. The absorbance of final sample solution was noted at 285 nm and 320 nm. The content of Ilaprazole was calculated by extrapolation from linearity equation at 320nm. The absorbance contribution of Ilaprazole at 285 nm was calculated from its linearity equation and correction was applied to know absorbance due to Domperidone. Concentration of Domperidone in sample was calculated from its linearity equation.

DISCUSSION

Absorbance correction method:

If a sample contains two absorbing drugs, which absorb light at either drug's $\lambda_{max,}$ it is possible to determine the drug by the technique of simultaneous equations – Vierodts method, or by ARM – Absorption Ratio Method or by ACI – Absorbance Corrected for Interference.

Principle of ACI: If the identity, concentration, and absorptivity of the absorbing interferences are known, it is possible to calculate their contribution to the total absorbance of a mixture. The Concentration of the component absorbing light can then be calculated from the total absorbance[11].

To determine the absorption of Domperidone in a mixture of Ilaprazole and Domperidone, a wavelength where Domperidone has negligible absorption was found, which was 320nm. It was observed that Domperidone absorbs no light at 320nm whereas Ilaprazole does.

Thus, when absorbance of mixture is determined at 320 nm, only Ilaprazole contributes. Its contribution at 285 nm can be calculated and subtracted to obtain absorbance due to Domperidone. Thus absorbtion correction is applied.

The accuracy results were found to be within limit of 98-102% recovery when freshly prepared solutions were used. But when the stock solutions of both Domperidone and Ilaprazole were kept in refrigerator (observed for a week) and used for further dilutions, slight deviation from limits was observed. The details are given below. Hence it will be advisable to use freshly prepared solutions, especially of Domperidone.

Validation of the method[12]:

The method was validated as per ICH Q2(R1) guidelines for linearity, accuracy, precision, LOD, and LOQ.

Parameters	Domperidone	Ilaprazole
Linearity range(mcg/ml)	25 to 75	10 to 50
Slope	0.0238	0.028
Intercept	0.151	0.011
Correlation coefficient	0.991	0.964
LOD (mcg/ml)	4.633	1.85
LOQ (mcg/ml)	14.04	5.61
Accuracy (% recovery)	103.2	101.7
Repeatability (%RSD)	1.73	2.1

ADVANTAGE:

Sample solutions were diluted using distilled water and their absorbances were measured. The absorbances

obtained using water and methanol as a solvent separately were found to be comparable. Hence using water was found to be economical.

CRITICAL OBSERVATION:

Domperidone degrades fast and hence the samples prepared have to be used immediately.

CONCLUSION

The developed ACI (Absorbance Corrected for Interference) method is simple, accurate and fast. It can be used for routine analysis of Domperidone and Ilaprazole in combination.

ACKNOLEWGDEMENT

REFERENCE:

1. Indian Pharmacopoeia, Volume II, The Controller of Publications, Govt. Of India, New Dlehi, (2014), pg. 1612

2. Indian Pharmacopoeia, Volume II, The Controller of Publications, Govt. Of India, New Dlehi, (2014), pg. 1947

3. Suneetha G, Venkateswarlu P, Dtermination of Ilaprazole and Domperidone in individual dosage form tablets by RP-HPLC, Asian Journal of Chemistry, 2013; 25(7): 3989-3992.

4. Pradhan PK, Mavani D., RP-HPLC method development and validation for simultaneous estimation of Ilaprazole and Domperidone in their combined dosage form, Journal of Drug Delivery and Therapeutics, 2014, 4(4): 43-48.

5. PrajapatiKM, PatelG, Prajapati B and ShahSK, Simultaneous Estimation of Ilaprazole and Domperidone in Pharmaceutical Dosage Form, International Journal of Pharmaceutical Sciences and Nanotechnology, 2016, 9(6): 3549-3555.

6. Patel PM, Sagar GV, Stability Indicating Chromatographic Method Development and Validation for the Simultaneous Determination of Ilaprazole and Domperidone in Its Pharmaceutical Dosage Form by RP- HPLC, Journal of Pharmaceutical and Medicinal Chemistry, 2016, 2(1): 85-93.

7. Patel PM, Desai VK, Stability Indicating Chromatographic Method Development And Validation for The SimultaneousEstimation of Ilaprazole And Domperidone in itsPharmaceutical Dosage Form By Hplc, Indian Journal of Research, 2016, 5(4): 107-108.

8. Sakhare RS, Pekamwar SS, Development and validation of stability indicating HPTLC method for simultaneous estimation of Ilaprazole and Domperidone in bulk and solid dosage form, International Journal of Pharmaceutical Sciences Review and Research, 2016, 41(2): 116-120.

9. Tayde V, Deshpande P, Validated Stability-indicating HPTLC Method for Simultaneous Estimation of Ilaprazole and Domperidone as Bulk Drugs and in Capsule Dosage Form, Acta Velit, 2017, 3(4):13-22.

10. GirirajP, SivakkumarT., Simultaneous Estimation of Domperidone and Ilaprazole in Pure and Capsule Dosage Form by Vierordt's Method. Inventi Impact: Pharm Analysis & Quality Assurance, 2014, (4):243-247, 2014.

11. Beckett A, Stenlacke J, Practical of pharmaceutical Chemistry Part 2, CBS Publishers, 1997: 1, 284, 279, 283, 284.

12. ICH, Q2 (R1) Validation of Analytical Procedure: Text and Methodology: International Conference on Harmonization (2005).