SIMULTANEOUS ESTIMATION OF LANSOPRAZOLE AND DOMPERIDONE IN TABLET DOSAGE FORM BY RP-HPLC

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ABSTRACT:
A RP-HPLC method has been developed in order to develop a new analytical method for simultaneous estimation of Lansoprazole and Domperidone by RP-HPLC. It is a specific blocker of dopamine receptors. It speeds gastrointestinal peristalsis, causes prolactin release, and is used as antiemetic and tool in the study of dopaminergic mechanisms. It acts as a gastrointestinal emptying (delayed) adjunct and peristaltic stimulant. Lansoprazole is a proton pump inhibitor which prevents the stomach from producing acid. It is manufactured by TAP pharmaceutical products. Column: Xterra C18 (4.6 x 250mm, 5µm, Make: Waters) was used to analyse LNP and DMP using Phosphate buffer (0.05M) pH 4.6; ACN (55:45%v:v) as mobile phase. The detection was carried out at274 with flowrate 1ml/min. The retention times obtained for LNP and DMP were 2.399mins and 3.907mins respectively. Linearity obtained was within the range of 1µg-5µg for Lansoprazole and 100µg-500µg for Domperidone and the Regression Co-efficient obtained was of 0.999 for both drugs. The detection was done using PDA detector at ambient temperature. The proposed method was validated for all the validative parameters and were found to be good accordance with ICH guidelines. Hence the developed method can be successfully applied for simultaneous estimation of Lansoprazole and Domperidone in routine analysis.

Keywords: RP-HPLC, Lansoprazole (LNP), Domperidone (DMP)

INTRODUCTION
Domperidone chemically is 5-chloro-1-[[1-(2-oxo-2, 3-dihydro-1H-1, 3-benzodiazol-1-yl) propyl] piperidin-4-yl]-2, 3-dihydro-1H-1, 3-benzodiazol-2-one which is used as specific blocker of dopamine receptors. It speeds gastrointestinal peristalsis, causes prolactin release, and is used as antiemetic and tool in the study of dopaminergic mechanisms. Lansoprazole chemically is 2-({[3-methyl-4-(2, 2, 2-trifluoroethoxy) pyridin-2-yl] methane} sulfinyl)-1H-1, 3-benzodiazole and used as a proton pump inhibitor which prevents the stomach from producing acid [1-2].

Literature survey reveals that there are methods to analyse these drugs by spectroscopic methods [3-4], in tablet [5-16], in plasma [17-18]. There are no methods reported in tablets using Buffer and Acetonitrile as solvent which is cost effective.

Hence an attempt is made to develop simple, Accurate and Precise and cost effective method [19-20] for simultaneous estimation of Lansoprazole and Domperidone by RP-HPLC in tablet dosage form according to ICH guidelines [21].
EXPERIMENTAL:

Table No1: instruments employed for the present work

| S.No. | Instrument                      | Model No.       | Software   | Manufacturer’s name |
|-------|---------------------------------|-----------------|------------|---------------------|
| 1     | HPLC Alliance PDA Detector      | Waters 2695     | Empower    | Waters              |
| 2     | UV double beam spectrophotometer| UV 3000         | UV Win 5   | Lab India           |
| 3     | Digital weighing balance        | BSA224SCW       | -          | Satorius            |
| 4     | pH meter                        | AD102U          | -          | Lab India           |
| 5     | Ultra sonicator                 | SE60US          | -          | -                   |
| 6     | Suction pump                    | VE115N          | -          | -                   |

Table No2: The reagents used for the present study

| S.No. | Chemical                                      | Manufacturer | Grade           |
|-------|-----------------------------------------------|--------------|-----------------|
| 1     | Water                                         | Merck        | HPLC Grade      |
| 2     | Methanol                                      | Merck        | HPLC Grade      |
| 3     | Acetonitrile                                  | Merck        | HPLC Grade      |
| 4     | Potassium dihydrogen fed orthophosphate       | Merck        | A.R             |
| 5     | Lansoprazole & Domperidone API                | -            | -               |
| 6     | Eurepa mf tablets                             | Local Pharmacy| -               |

ANALYTICAL METHOD DEVELOPMENT:

Method development for simultaneous estimation of Lansoprazole and Domperidone in Pharmaceutical dosage forms includes the following steps:

1. Selection of detection wavelength ($\lambda_{\text{max}}$)
2. Selection of column
3. Selection of mobile phase
4. Selection of flow rate
5. Preparations and procedures

1. Selection of Detection wavelength:

10 mg of Lansoprazole and Domperidone was dissolved in mobile phase. The solution was scanned from 200-400 nm the spectrum was obtained. The overlay spectrum was used for selection of wavelength for Lansoprazole and Domperidone. The isobestic point was taken at 255nm as detection wavelength. The overlay spectrum is in the figure-1.
2. Selection of column:
Column is selected based on solubility, polarity and chemical differences among analytes. Column selected for present study is [Column: Xterra C18 (4.6 x 250mm, 5µm, Make: Waters)]

3. Selection of mobile phase:
Phosphate buffer (0.05M) pH 4.6: ACN (55:45%v/v) has been selected as mobile phase. Buffer pH should be between 2 to 8. If the buffer pH is below 2 siloxane linkages are cleaved. If the buffer pH is above 8 dissolution of silica takes place. pH controls the elution properties by controlling the ionization characteristics. It also decreases the retention and improves separation. Good Response, Area, Tailing factor, Resolution will be achieved.

4. Selection of flow rate:
Flow rate selected was 1ml/min
Flow rate is selected based on
1. Retention time
2. Column back pressure
3. Peak symmetry
4. Separation of impurities.

Assay Calculations for Lansoprazole and Domperidone.
The assay study was performed for the Lansoprazole and Domperidone. Each two injections of sample and standard was inject into chromatographic system and results are in table-3

VALIDATION OF PROPOSED METHOD:
The % purity of Lansoprazole and Domperidone in pharmaceutical dosage form was found to be 100.7% and 101.4% respectively.

Validation results.
1. Accuracy:
The accuracy study was performed for 50%, 100% and 150 % for Lansoprazole and Domperidone. Each level was injected in triplicate into chromatographic system. The area of each level was used for calculation of % recovery and results are listed in table-4

2. PRECISION:
Precision was performed for five injections of Lansoprazole and Domperidone. Each standard was injected into chromatographic system. The area of each Standard injection was used for calculation of % RSD and results are listed in table-5

RP-HPLC DATA OF DRUGS

![Figure No: 2 RPHPLC Chromatogram of Standard Lansoprazole and Domperidone](image)
**Table No 3: Calculations for Lansoprazole and Domperidone**

| Name: Lansoprazole | Name | RT  | Area     | USP Plate Count | USP Tailing | USP Resolution |
|--------------------|------|-----|----------|-----------------|-------------|----------------|
| 1                  | Lansopra | 3.525 | 810802   | 3527.8          | 1.0         | 2.4            |
| 2                  | Lansopra | 3.528 | 808790   | 3566.2          | 1.0         | 2.3            |
| Mean               |       |      | 809796   | 3547.0          | 1.0         |                |
| Std. Dev.          |       |      |         |                 |             |                |
| % RSD              |       |      |         |                 | 0.18        |                |

| Name: Domperidone  | Name  | RT  | Area     | USP Plate Count | USP Tailing |
|--------------------|-------|-----|----------|-----------------|-------------|
| 1                  | Domperi | 2.984 | 681469   | 3115.4          | 1.1         |
| 2                  | Domperi | 2.989 | 683696   | 3209.7          | 1.1         |
| Mean               |       |      | 682582   | 3162.5          | 1.1         |
| Std. Dev.          |       |      |         |                 | 0.23        |
| % RSD              |       |      |         |                 |             |

**Table No 4: Accuracy results of Lansoprazole**

| % Concentration (at specification level) | Area | Amount Added(mg) | Amount Found(mg) | % Recovery | Mean Recovery |
|-----------------------------------------|------|------------------|------------------|------------|---------------|
| 50%                                     | 644765 | 5                | 5.0              | 101.3%     |               |
| 100%                                    | 803722 | 10               | 9.94             | 99.4%      | 100.0%        |
| 150%                                    | 962917 | 15               | 14.8             | 99.2%      |               |

**Table No 5: Calculation of % RSD**

| Name: Lansoprazole | Name | RT  | Area    |
|--------------------|------|-----|---------|
| 1                  | Lansopra | 3.557 | 819305  |
| 2                  | Lansopra | 3.547 | 807157  |
| 3                  | Lansopra | 3.544 | 804070  |
| 4                  | Lansopra | 3.537 | 808474  |
| 5                  | Lansopra | 3.534 | 804505  |
| Mean               |       |      | 808702  |
| Std. Dev.          |       |      |         |
| % RSD              |       |      | 0.77     |

| Name: Domperidone  | Name | RT  | Area    |
|--------------------|------|-----|---------|
| 1                  | Domper | 3.019 | 691143  |
| 2                  | Domper | 3.011 | 685431  |
| 3                  | Domper | 3.004 | 683543  |
| 4                  | Domper | 2.997 | 683564  |
| 5                  | Domper | 2.994 | 683532  |
| Mean               |       |      | 685443  |
| Std. Dev.          |       |      | 3289.7  |
| % RSD              |       |      | 0.48     |
The Method precision study was performed for the %RSD of Lansoprazole and Domperidone was found to be 0.7 and 0.4 (NMT 2).

3. Intermediate precision/Ruggedness

The intermediate precision study was performed for five injections of Lansoprazole and Domperidone. Each standard injection was injected into chromatographic system. The area of each standard injection was used for calculation of %RSD.

**Table No 6: Intermediate precision/Ruggedness of Lansoprazole and Domperidone**

| Name: Lansoprazole | Name | RT | Area    |
|--------------------|------|----|---------|
| 1                  | Lansop | 3.524 | 813507  |
| 2                  | Lansop | 3.533 | 817673  |
| 3                  | Lansop | 3.533 | 815189  |
| 4                  | Lansop | 3.517 | 815816  |
| 5                  | Lansop | 3.530 | 815356  |

Mean: 815508

Std. Dev.: 1492.7

% RSD: 0.18

| Name: Domperidone | Name  | RT | Area    |
|-------------------|-------|----|---------|
| 1                 | Domper | 3.001 | 673725  |
| 2                 | Domper | 3.009 | 672535  |
| 3                 | Domper | 3.010 | 676216  |
| 4                 | Domper | 2.997 | 679037  |
| 5                 | Domper | 3.007 | 677101  |

Mean: 675723

Std. Dev.: 2611.5

% RSD: 0.39

The intermediate precision was performed for %RSD of Lansoprazole and Domperidone was found to be 0.18 and 0.39 respectively (NMT 2).

4. Specificity:

The system suitability for specificity was carried out to determine whether there is any interference of any impurities in retention time of analytical peak. The study was performed by injecting blank.

**Injection Detection of limit:**

LOD’s can be calculated based on the standard deviation of the response (SD) and the slope of the calibration curve (S) at levels approximating the LOD according to the formula. The standard deviation of the response can be determined based on the standard deviation of y-intercepts of regression lines.

**Linearity:**

The linearity study was performed for the concentration of 100ppm to 500ppm and 1ppm to 5ppm level. Each level was injected into chromatographic system. The area of each level was used for calculation of correlation coefficient.

The linearity study was performed for concentration range of 1μg - 5μg and 100μg-500μg of Lansoprazole and Domperidone and the correlation coefficient was found to be 0.999 and 0.999 (NLT 0.999).

**Table No 6: Linearity results of Domperidone**

| S.No | Linearity | Level | Concentration | Area   |
|------|-----------|-------|---------------|--------|
| 1    | I         | 100ppm| 226418        |
| 2    | II        | 200ppm| 432920        |
| 3    | III       | 300ppm| 677256        |
| 4    | IV        | 400ppm| 869825        |
| 5    | V         | 500ppm| 1095759       |

Correlation Coefficient: 0.999

**Acceptance Criteria:**
Correlation coefficient should be not less than 0.999

**Linearity Results (for Lansoprazole):**

**Table No 7: Linearity results of Lansoprazole**

| S.No | Linearity | Level | Concentration | Area   |
|------|-----------|-------|---------------|--------|
| 1    | I         | 1ppm  | 277182        |
| 2    | II        | 2ppm  | 521695        |
| 3    | III       | 3ppm  | 808274        |
| 4    | IV        | 4ppm  | 1033875       |
| 5    | V         | 5ppm  | 1285804       |

Correlation Coefficient: 0.999

**Acceptance Criteria:**
Correlation coefficient should be not less than 0.999.
The LOD was performed for Lansoprazole and Domperidone was found to be 2.95 and 3.04 respectively.

The LOQ was performed for Lansoprazole and Domperidone was found to be 9.87 and 10 respectively.
**Conclusion:**

An attempt was made in order to develop a simple, accurate and cost effective analytical method to simultaneously estimate Domperidone and Lansoprazole in tablet dosage form by RP-HPLC using Phosphate buffer and Acetonitrile in 45:55 ratios. The method was found to be accurate, precise and robust. Linearity studies were done in which Regression co-efficient was 0.999 for both drugs. The method was validated according to ICH guidelines and RSD, %RSD were less than one which states that the proposed method was in fair agreement. Hence the proposed method can be used for routine analysis of Domperidone and Lansoprazole in Pharmaceutical preparations.

**References:**

1. British Pharmacopoeia 1999; Volume-I:545-546.
2. Sethi PD. HPLC: Quantitative Analysis of Pharmaceutical Formulations. CBS Publications, New Delhi, India, 1996.
3. Saudagar RB, Saraf S, Saraf S. First order Derivative simultaneous equation and area under the curve methods for estimation of Domperidone maleate and Rabeprazole sodium in tablet dosage form. Indian Drugs. 2006;43(5):388-392.
4. Meyyanathan SN, Avavinda Raj JR,Suresh B. Spectrophotometric determination of Lansoprazole in its dosage forms. Indian Drugs. 1997;34(7):403-406.
5. Santhosha B, Ravindranath A, Sundari CH. Stability indicating RP-HPLC method for the simultaneous estimation of domperidone and lafutidine in bulk and the pharmaceutical dosage form. Int J Pharm Pharm Sci. 2012;4(4):589-594.
6. Sumithra M, Ravichandiran V, Dammayi D, Shanmugasundaram P, Sankar ASK. Method development and validation for simultaneous estimation of pantoprazole and domperidone in pharmaceutical dosage form. J Pharm Res. 2012;5(9):4697-4700.

7. Ahmed S, Vani R. Stability indicating method development and validation for simultaneous estimation of lansoprazole and domperidone in bulk and its pharmaceutical dosage form by RP-HPLC. World J Pharm Pharm Sci. 2014;4(1):656-665.

8. Janardhanan VS, Manavalan R, Valliappan K. Stability-indicating HPLC method for the simultaneous determination of pantoprazole, rabeprazole, lansoprazole and domperidone from their combination dosage forms. Int J Drug Dev Res. 2011;3(4):323-335.

9. Singh S, Choudhary N, Rai J, Siddiqui I, Sharma S. A validated RP-UPelC method development for simultaneous estimation of lansoprazole and naproxen in bulk and tablet dosage form. Asian J Pharm Clin Res. 2013;6(4):150-152.

10. Suparna S, Kumar SA, Ompal S, Kumar CA, Vikrant V, Kumar AR et al. RP-HPLC Method Development and Validation of Domperidone in Solid Dosage Form. The Pharm Innov. 2012;1(4):16-20.

11. Birajdar AS, Meyyanathan SN, Suresh B. Application of UV-Spectrophotometry and RP-HPLC for Simultaneous Determination of Rabeprazole and Domperidone in Pharmaceutical Dosage Form. Der Pharmacia Sinica. 2010;1(3):69-78.

12. Ramadan NK, Mohamed HM, Moustafa AA. Simultaneous determination of Rabeprazole sodium and Domperidone. J Appl Pharm Sci. 2011;1(9):73-80.

13. Sai MP, Rajesh B, Patnaik A, Shankar CH, Kumar YK. Simultaneous estimation of Rabeprazole and Domperidone in dosage forms by RP-HPLC. Int J Res Pharm Sci. 2014;5(4):259-261.

14. El-Fatatry HM, Mabrouk MM, Hewala II, Emam EH. Stability-indicating HPLC–DAD methods for determination of two binary mixtures: Rabeprazole sodium–mosapride citrate and rabeprazole sodium–itopride hydrochloride. J Pharm Anal. 2014;4(4):258-269.

15. Thakkar DG. Development and Validation of UV Spectroscopic and RP-HPLC method for Simultaneous Estimation of Levosulpiride and Rabeprazole Sodium in bulk and tablet dosage form. J Pharm Sci Biosci Res. 2013;3(3):108-114.

16. Antala H. Development and validation of RP-HPLC method for the simultaneous estimation of Lafutidine and Rabeprazole Sodium in combined dosage form. Int J Pharm Pharm Sci. 2013;5(4):975-1491.

17. Ograhic analysis for the determination of domperidone in human plasma. J Chromatogr B Biomed Sci Appl. 2000;744(1):207-212.

18. Yamamoto K, Hagi M, Kotaki H, Igu T. Quantitative determination of domperidone in rat plasma by high-performance liquid chromatography with fluorescence detection. J Chromatogr Biomed Sci Appl. 1998;720(1-2):251-255.

19. Snyder LR, Kirkland JJ, Glajch JL. Practical HPLC method development. John Wiley & Sons; 2013:1-56.

20. Singh R. HPLC method development and validation-an overview. J Pharm Edu Res. 2013;4(1):26.

21. Taleuzzaman M, Ahmed MM, Chattopadhyaay M. Particle size role, importance and strategy of HPLC Analysis – An update. Int Arch Biomed Clin Res. 2016;2(2):5-11.

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