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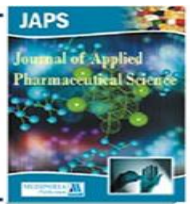

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Development and Validation of RP-HPLC Method for the Simultaneous Estimation of Domperidone and Naproxen in Tablet Dosage Form

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ABSTRACT

A simple, selective and rapid reversed phase High Performance Liquid Chromatographic (RP-HPLC) method has been developed and validated for the simultaneous analysis of domperidone and naproxen in tablet dosage form. The chromatographic system consisted of two LC-20 AT pump, SPD-20A UV detector, SIL-20A auto-sampler and CTO-10ASVP column oven. Chromatographic separation of drugs was achieved on an Shim-Pack C_{18} column (250 mm x 4.6 mm, 5 µm) as stationary phase with a mobile phase comprising of phosphate buffer (pH adjusted to 3.00 with sodium hydroxide): methanol in the ratio 30:70 (v/v) at a flow rate of 1.0 ml/min with UV detection at 280 nm. Retention time was 3.17 minutes for domperidone and 5.42 minutes for naproxen. The method was found selective and peaks of domperidone and naproxen were well separated (resolution 10.72). The proposed method is linear (r^2 = 0.999 for domperidone and naproxen), accurate with 99.5% recovery for domperidone and 99.39% recovery for naproxen and precise (%RSD < 1%). The method has been used to determine potency of commercial product and potency was found within limit. The method can be used for the analysis of domperidone and naproxen in tablet dosage form.

Key words: *Domperidone, naproxen, validation, RP-HPLC, quantitative analysis.*

INTRODUCTION

Reversed-phase high performance liquid chromatography (RP-HPLC) is very useful for simultaneous determination of drugs in pharmaceutical dosage forms. This technique is widely used for higher sensitivity and selectivity. This paper describes a simple reverse phase high performance liquid chromatographic method (RP-HPLC) for simultaneous estimation of domperidone and naproxen in tablet dosage form. Chemically Domperidone is 5- chloro- 1- [1- [3- (2- oxo- 2, 3- dihydro- 1H-benzimidazol- 1- yl) propyl]- piperidin- 4- yl]- 1, 3- dihydro- 2H benzimidazol- 2- one and Naproxen (NAP) is (2*S*)-2-(6-Methoxynaphthalen-2-yl) propanoic acid. Domperidone is a D_2 receptor antagonist. It increases gastrointestinal peristalsis and motility that prevent reflux esophagitis and it is used to prevent nausea and vomiting. Naproxen is a well-known non-steroidal anti-inflammatory drug which is clinically used in treatment of rheumatoid arthritis and other painful musculoskeletal disorders. It works by inhibiting both the COX-1 and COX-2 enzymes. Several analytical procedures have been proposed for the quantitative estimation of domperidone and naproxen separately and in combination with other drugs. HPLC (Varalakshmi et al, 2011) and UV (Rajendra et al , 2009) methods for estimation of domperidone alone in pharmaceutical preparation have been reported.

Domperidone in combination with Lansoprazole (Bhavna et al, 2009), Pantoprazole (Sivakumar et al, 2008), Rabeprazole (Kalirajan et al, 2007) omeprazole (Laksmi et al, 2007) and paracetamol (Karthik et al, 2007) are also available.

Naproxen in combination with other drugs is estimated by UV (Tasnuva et al, 2007) and HPLC (Haque et al, 2010) have also been reported.

To our knowledge simple and economical analytical method for simultaneous determination of domperidone and naproxen has not been reported so far. So attempt was taken to develop and validate an economic, rapid reversed-phase high performance liquid chromatographic method for the quality control of domperidone and naproxen in pharmaceutical preparations with lower solvent consumption along with the short analytical run time that leads to an environmentally friendly chromatographic procedure and will allow the analysis of a large number of samples in a short period of time. The method was validated and found to be accurate, precise and reproducible.

MATERIAL AND METHODS

Apparatus

A Shimadzu (Japan) HPLC system consisting of a CMB-20 Alite system controller, two LC-20AT pumps, SIL-20A auto-sampler and CTO-10ASVP column oven were used. Ultraviolet detection was achieved with a SPD-20A UV-VIS detector (Shimadzu, Japan). The drug analysis data were acquired and processed using LC solution (Version 1.2, Shimadzu, Japan) software running under Windows XP on a Pentium PC.

Reagents and chemicals

Domperidone and naproxen were kind gift from incepta Pharmaceuticals Limited Dhaka, Bangladesh. Methanol was of HPLC grade and collected from E. Merck, Darmstadt, Germany. Dipotassium hydrogen phosphate and Potassium dihydrogen ortho-phosphate were analytical reagent grade supplied by M/S Qualigens Fine Chemical. Sodium hydroxide was of analytical reagent grade from Ranbaxy Laboratories Ltd. Water was deionised and double distilled

Commercial formulation

Combination products of domperidone and naproxen were not available in our local market currently. Domilux (10 mg domperidone) tablets and Naspro (250 mg naproxen) were purchased from local drug store in Dhaka city. The samples were properly checked for their manufacturing license numbers, batch numbers, production, expiry dates and stored properly.

Preparation of standard solution

20 mg domperidone was dissolve in 100 ml mobile phase and 25 mg naproxen was dissolve in 25 ml mobile phase separately to get stock solutions of domperidone (200 mcg/ml) and naproxen (1000 mcg/ml). Several aliquots of standard solutions of domperidone and naproxen were taken in different 100 ml volumetric flasks and diluted up to the mark with mobile phase to get five different concentrations (80%, 90%, 100%, 110% and 120% of target concentration). Solution containing mixture of domperidone and naproxen of five different concentrations (80%, 90%, 100% 110%, and 120% of target concentration) were prepared in the same way.

Preparation of sample solution

Sample solution containing both the drugs was prepared by dissolving tablet powder into mobile phase. Twenty Domilux tablets and Naspro tablets were weighed separately. Their average weights were determined. Powder of tablets equivalent to 5 mg of domperidone and 125 mg of naproxen were weighed and taken in a 100 ml volumetric flask, dissolved in mobile phase and shaken for about 10 minutes then filtered through filter paper. The filtered solution was further diluted in the mobile phase to make the final concentration of working sample equivalent to 100% of target concentration.

Chromatographic conditions

The mobile phase, a mixture of phosphate buffer and methanol (30:70v/v) pumped at a flow rate of 1.0 ml/min through the column (C_{18}; 5µ, 4.6 X 250 mm, shim Pack, Japan) at 30^0C. The mobile phase was degassed prior to use under vacuum by filtration through a 0.2µ nylon membrane. Concentrations were measured at 280 nm by UV detector at a sensitivity of 0.0001.

Development and validation of HPLC method

Present study was conducted to obtain a new, affordable, cost-effective and convenient method for HPLC determination of domperidone and naproxen in tablet dosage form. The experiment was carried out according to the official specifications of USP–30, ICH- 1996 and Global Quality Guidelines-2002.The method was validated for the parameters like system suitability, selectivity, linearity, accuracy, precision and robustness.

System suitability

System suitability study of the method was carried out by six replicate analysis of solution containing 100% target concentration of domperidone and naproxen. Various chromatographic parameters such as retention time, peak area tailing factor, theoretical plates (Tangent) of the column and resolution between the peaks were determined and the method was evaluated by analyzing these parameters.

Selectivity

Selectivity test determines the effect of excipients on the assay result. To determine the selectivity of the method, standard sample of domperidone and naproxen were injected first. Then commercial product, blank and excipients solution were run in the instrument one after another.

Linearity

Linearity of the method was determined by constructing calibration curves. Standard solutions of domperidone and naproxen of different concentrations level (80%, 90%, 100%, 110%, and 120%) were used for this purpose. Each measurement was carried out in six replicates and the peak areas of the

chromatograms were plotted against the concentrations to obtain the calibration curves and correlation coefficients.

Accuracy

Spike and recovery method was used to determine the accuracy of the method. Both the drugs at different level were added to placebo formulations. The accuracy was calculated as the percentage of the dug recovered by the assay.

Precision

Intra-day precision (repeatability) was determined by performing four repeated analysis of the three standard solutions (90%, 100% and 110% of target concentration) on the same day. On the other hand inter-day precision (intermediate) of the method was assessed by carrying out the analysis of standard solutions (90%, 100% and 110% of target concentration) on three different days in the same laboratory. The relative standard deviation (% RSD) was calculated in order to assess the precision of the method.

Robustness

Robustness of the method was determined by the analysis of the samples under a variety of conditions. Small changes were made in the buffer pH (2.8 and 3.0), mobile phase composition, flow rate (0.9 and 1.1/min) and in temperature (30 ºC and 28 ºC). Percent recovery was calculated to find out the robustness of the method.

RESULTS AND DISCUSSION

Results of system suitability study are summarized in Table 1. Six consecutive injections of the standard solution showed uniform retention time, theoretical plate count, tailing factor and resolution for both the drugs which indicate a good system for analysis.

Table 1: Result of system suitability tests of domperidone and naproxen.

Parameters	Domperidone			Naproxen		
	Average	SD	%RSD	Average	SD	%RSD
Retention time	3.168	0.001	0.041	5.424	0.004	0.076
Area	125978.00	1249.903	0.992	1622441.500	376.285	0.023
Theoretical plates	4561.153	18.792	0.412	8739.667	5.750	0.066
Tailing factor	1.357	0.004	0.287	1.355	0.015	1.090
Resolution				10.719	0.018	0.168

Chromatograms shown in figure 1 explain that retention time for standard sample and commercial product of domperidone and naproxen are same. This proves that, excipients have no effect on the analytical method. On the other hand, blank peak did not overlap drug peak. So the method is highly selective. A linear relationship between peak areas (average peak areas of six replicates) *versus* concentrations was observed for domperidone and naproxen in the range of 80% to 120% of nominal concentration. Correlation coefficient was 0.999 for both the drugs which prove that the method is linear. Calibration curve of domperidone and naproxen are shown in Fig 2 and 3.

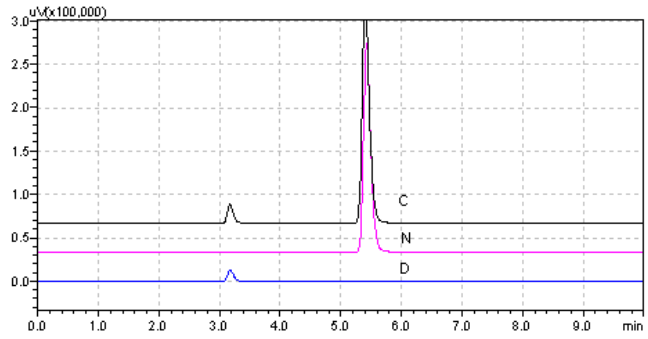

Fig: 1 Chromatogram of domperidone (D), naproxen (N) and commercial product (C).

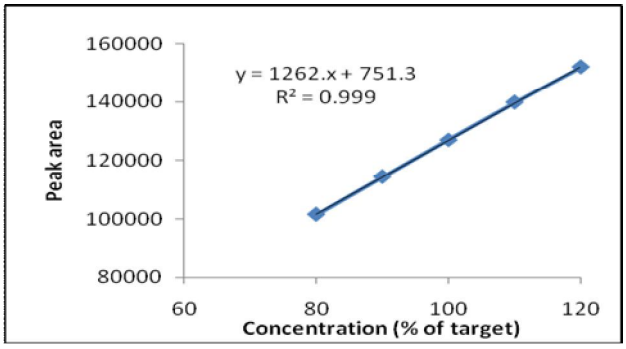

Fig: 2 Calibration curve of domperidone.

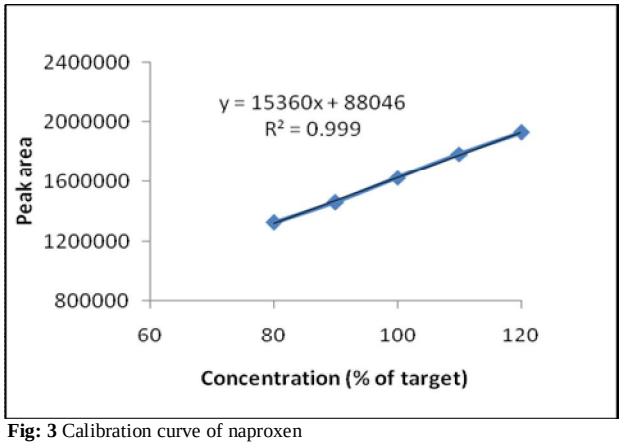

Fig: 3 Calibration curve of naproxen

Table 2: Accuracy (%recovery) results of domperidone and naproxen.

Sample no.	Domperidone			
	Spiked amount(mg)	Recovered amount (mg)	% recovered	% Average recovery
1	10.00	9.79	97.90	
2	15.00	14.85	99.00	99.50
3	20.00	20.32	101.60	
Sample no.	Naproxen			
	Spiked amount(mg)	Recovered amount(mg)	% recovered	% Average recovery
1	15.00	14.31	95.40	
2	22.50	22.87	101.64	99.39
3	30.00	30.34	101.13	

Results of accuracy study are presented in table 2. The measured value was obtained by recovery test. Spiked amount of both the drug were compared against the recovery amount.

% Recovery was 99.50% for domperidone and 99.39% for naproxen. All the results indicate that the method is highly accurate. Results of Intra day and inter day variability were summarized in table 3. Intra day variability was done from 9.00 am to 6.00 pm on the same day. % RSD of peak areas was calculated for various run .The method is highly precise as % RSD of peak area was less than 1% in all tests.

Table 3: Intra day and inter day precision result of domperidone and naproxen.

Drug	% RSD (intra day)	% RSD (inter day)
Domperidone	0.929	0.824
Naproxen	0.054	0.374

The results of robustness of the present method showed that small changes were made in the buffer pH, mobile phase composition, flow rate and temperature did not produce significant changes in analytical results which are presented in Table 4. As the changes are not significant we can say that the method is robust

Table 4: Results for robustness test of domperidone and naproxen

Parameters	Changes	% Recovery of domperidone	% Recovery of naproxen
Flow rate (ml/min)	0.9	98.89	98.71
	1.1	99.19	99.14
Column temperature (0C)	28	99.27	99.64
	30	99.13	99.59
Methanol variation	70%	99.19	99.70
	72%	98.80	99.68
pH	3.00	99.12	99.74
	2.80	98.87	99.62

The proposed method was used to determine the potency of commercially available tablets. Potency of domperidone tablet (10 mg) and naproxen tablet (250 mg) were determined. Tablet powder was mixed and solution containing both drugs was prepared. Six replicate determinations were carried out and the results are summarized in Table 5.

Table 5: Potency of domperidone and naproxen in tablets.

Drug	Label claim (mg)	Observed amount (mg) (n=6)	Potency (%)
Domperidone	10.00	9.89	98.90
Naproxen	250.00	248.45	99.38

CONCLUSION

The proposed high-performance liquid chromatographic method has been evaluated for the accuracy, precision and linearity. The measured signals were shown to be precise, accurate and linear over the concentration range tested (80–120% of target concentration) with a correlation coefficient of 0.999. In this method, there was no interference from matrix sources. Moreover, the lower solvent consumption along with the short analytical run time of 10 minutes leads to an environmentally friendly chromatographic procedure that allows the analysis of a large number of samples in a short period of time. Therefore, this HPLC method can be used as a routine sample analysis.

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