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Validated RP-HPLC Method for Simultaneous Estimation of Domperidone and Naproxen in Bulk Drug and Formulations

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Abstract— A new , precise , accurate and reproducible RP – HPLC method for simultaneous estimation of bulk and pharmaceutical formulations . Separation of Naproxen and Domperidone was successfully achieved. THERMO HYPERSIL , C 18 , 250mm X 4.6mm , 5µm , or equivalent in an isocratic mode utilizing Acetonitrile : Methanol : Water (20: 60:20) at a flow rate of 1.0 mL/ min and elute was monitored at 284nm , with a retention time of 2.341 and 5.225 minutes for Naproxen and Domperidone respectively. The method was validated and the response was found to be linear in the drug concentration range of 1µg /mL to 6µg/mL. The values of correlation coefficient was found to be 0.988 for Naproxen and 0.998 for Domperidone respectively. The LOD and LOQ for Naproxen was found to be 0.56, 1.71 respectively . The LOD and LOQ for Domperidone was found to be 1.49 , 4.5 respectively. This method was found to be good percentage recovery for Naproxen and Domperidone were found to be 98% and 101.6% respectively indicates that the proposed method was highly accurate. The specificity of method shows good correlation between retention times of standard with the sample. The method was extensively validated according to ICH guidelines for Linearity , Accuracy , Precision , Specificity , and Robustness .

Keywords : Naproxen and Domperidone , High performance liquid chromatography

1. INTRODUCTION

Naproxen is an anti-inflammatory non-steroidal (NSAID) drug for the treatment of arthritis (Arthuris, rheumatic, juvenile arthritis) symptoms including inflammation, swelling, and joint pain (AA). Naproxen also helps to relieve the symptoms of ankylosing spondylitis, a type of arthritis that affects the joints of the spine. However, this medicine does not cure arthritis and will only help you as long as you continue to take it.

Domperidone is a medication that enhances movements or contractions of the stomach and bowel. It is also used to relieve nausea and vomiting caused by other medicines used in the treatment of Parkinson's disease. Domperidone is only prescribed under the guidance of doctors.

Easy and cost-effective analytical approaches have not been reported to our knowledge to date for the simultaneous determination of domperidone and naproxen. In pharmaceutical preparations with lower solvent consumption, an economic, rapid reversed-phase high-performance liquid chromatographic method for the quality control of domperidone and naproxen was therefore developed and validated along with the short analytical run time that leads to an environmentally friendly chromatographic process. The process was tested and found to be correct, correct and reproducible. Many analytical approaches have been proposed for the quantitative estimation of domperidone and naproxen separately and in combination with other drugs. HPLC (1,2) and UV (3) have documented the methods for estimating domperidone alone in pharmaceutical preparation. A mixture of Lansoprazole (4), Rabeprazole (5), paracetamol (6), omeprazole (7) and Ilaprazole(8) is also available with Domperidone. UV (9) and HPLC (10) estimations have also been released for naproxen in conjunction with other medications. A mixture of sumatriptan succinate, naproxen with Domperidone available(11,12), naproxen and domperidone(13-15), sumatripatan

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succinate and naproxen (16), review on naproxen (17,18).

2. MATERIALS AND METHODS

2.1 Chromatographic conditions

Column: ODS (4.6×250mm, 5µm, Hypersil)
Mobile phase: Acetonitrile: Methanol: Water (20:60:20)
Flow rate: 1ml/min
Column temperature: 35°C
Volume of injection: 10µl
λmax : 284nm

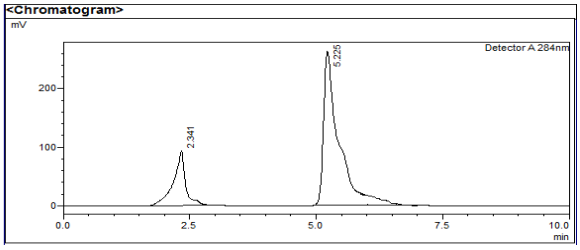

Fig1:Typical Chromatogram for optimized method

2.2 Degradation studies

The forced degradation was carried under acidic, basic, oxidative conditions. Both the drugs were separately exposed to stress conditions. After the exposing stresses conditions, drugs were diluted to the standard concentration of Naproxen (30µg/ml & 160µg/ml) and Domperidone (30µg/ml & 160µg/ml). Equal volume of the both the drugs were mixed and were analyzed in the developed method conditions. The acid catalyzed condition was provided to the drug by mixing the 1000µg/ml with the 2N HCl. The solution was diluted and left for 48hours and then injected into the chromatographic column, degradants evaluated using chromatograms. The alkali hydrolysis was carried out using 2N NaOH, when mixed with the drug solution and kept for 48hours and then injected into the chromatographic column the peaks were split into 4 peaks. Hydrogen peroxide is a strong oxidant when 3% H_2O_2 was added to the 1000µg/ml drug and kept for 48hours and injected into the chromatographic column in order to check the degradedness.

3. RESULTS AND DISSCUSSIONS

System suitability

System suitability is good enough due to similar observations of theoretical plates, resolution, tailing factor and retention time for Naproxen and Domperidone in six standard solution injections.

Specificity

There is no overlap between sample peak and blank peak and no interference of impurities in sample peak. Hence, this method is unique and selective.

Accuracy

Percentage recovery was 100.0% for Naproxen and 99% for Domperidone

Precision

% RSD is <2. % RSD for Naproxen & Domperidone was found to be 0.566 & 1.76

Linearity

Plot a graph between peak areas and concentration is a straight line for Naproxen and Domperidone in 1 – 6 µg/ml of concentration with correlation coefficients 0.998 and 0.988 respectively.

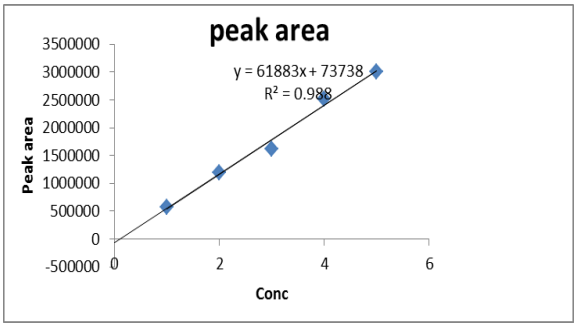

Fig2:Linearity plot of Domperidone

Solution No.	Concentration	Peak Area
1	1 µg/mL	575301
2	2 µg/mL	1198593

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3	3 µg/mL	1612737
4	4 µg/mL	2516911
5	5 µg/mL	3010328

Table 1:Linearity data for DOMPERIDONE

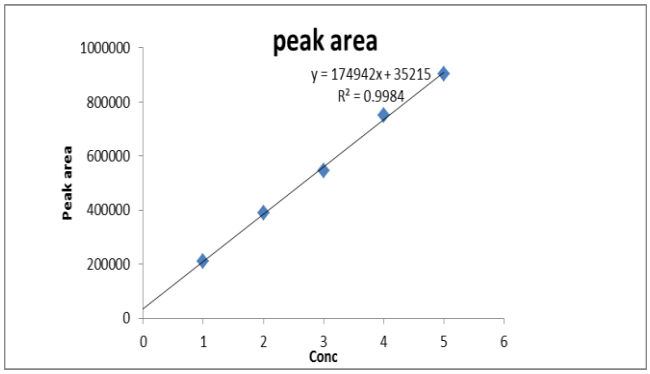

Fig 3:Linearity plot for Naproxen

Solution No.	Concentration	Avg. Area
1	1 µg/mL	209890
2	2 µg/mL	390059
3	3 µg/mL	545648
4	4 µg/mL	749951
5	5 µg/mL	904652

Table 2:Linearity data for NAPROXEN

Robustness

As the changes in flow rate and temperature did not produce any noticeable changes in results, the present method is Robust.

Limit of detection

LOD for Naproxen = 0.56

LOD for Domperidone= 1.49

Limit of quantification

LOQ for Naproxen = 1.71

LOQ for Domperidone = 4.5

Stability studies

Comparative studies were carried out on drugs called Naproxen and Domperidone before and after degradation and reported results of the drugs degraded on acid, base and oxidative, dry heat degradation.

Stress degradation study

Stress degradation properties were studied for the Naproxen and Domperidone by adopting validated chromatographic method.

Forced degradation studies are reported in Table. Reports show that the validated method has successfully separated the degradation products and identified separately. It is very clear from the reports that drugs were respond to the alkaline, oxidative and dry heat conditions where more degradation occurred.

Parameters	**HPLC Result**		**Acceptance criteria**
	Naproxen	**Domperidone**	
Specificity	No interference		No interference of excipients
Linearity			
Slope	17494	61883	
Intercept	35215	73738	
Correlation coefficient(r^2)	0.998	0.988	0.99
LOD	0.56µg/ml	1.49 µg/ml	-
LOQ	1.71 µg/ml	4.5 µg/ml	-
Accuracy			
50%	100.1 %	99.8%	98-102%
100%	98.7%	99.61%	
150%	100.3%	99.9%	
Precision			
System precision	1.03	2.00	2% (RSD)
Method Precision	0.12	0.18	2% (RSD)
System suitability			
Theoretical plates	4517.33	8652	NLT 2000
Tailing factor	0.801	1.678	NMT 2
RSD%	0.56	1.76	NMT 2%

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Table 3: Validation data for Naproxen & Domperidone

Sample	Degradation studies	Rt	Area	eoretical plates	iling factor
Naproxen	Acid Degradation-30µg/ml	1.629	7270	13441	1.724
	Acid Degradation-160µg/ml	1.844	15435	12958	-
	ali Degradation-30µg/ml	1.477	4840	5002	-
	Alkali Degradation-160µg/ml	1.487	2112	4187	1.386
	Oxidation -30µg/ml	6.016	17673	7401	-
	dation -160µg/ml	6.187	31794	9239	1.23
	Heat-30µg/ml	1.493	1443	4722	1.317
	Heat-160µg/ml	1.535	4382	3898	1.001
Domperidone	d Degradation-30µg/ml	4.536	60198	15579	1.238
	d Degradation-160µg/ml	4.547	109696	16431	1.263
	ali Degradation - 30µg/ml	1.804	235247	4129	-
	Alkali Degradation -160µg/ml	2.516	147525	5170	2.01
	Oxidation -30µg/ml	2.584	145705	11681	1.93
	Oxidation -160µg/ml	2.591	12730	11237	1.97
	Heat-30µg/ml	1.410	9708	3020	0.718
	Heat-160µg/ml	1.629	9898	4931	-

Table 4: Stress degradation data for Naproxen and Domperidone

CONCLUSION:

The author throws light on the improvement of HPLC methods for estimation of Naproxen and Domperidone in pharmaceutical formulations. Generally it is necessary to design methods in which a very large number of samples are to be analysed in very short span of time with reasonable precision and accuracy. Qualitative results can be obtained through HPLC method and thus it can be used in analytical analysis. This is an adequate method that gives good results in validation parameters. Specifically, this method performs well on Naproxen and Domperidone. The method is stability indicating that can be used without difficulty for the regular quality control analysis of Naproxen and Domperidone in industry studies.

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