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A NEW RP – HPLC METHOD FOR SIMULTANEOUS ESTIMATION OF NAPROXEN AND SUMATRIPTAN IN TABLET DOSAGE FORM

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ABSTRACT

A new simple fast accurate and economical reverse phase high performance liquid chromatographic method was developed for the determination of Naproxen Sodium [NPS] and Sumatriptan succinate [STS] in bulk and tablet dosage form. The separation was eluted on a Hypersil BDS C_{18} column (100 mm x 4.6 mm; 5µ) using a mobile phase mixture of phosphate buffer 6.5 and acetonitrile in a ratio of 60:40 v/v at a flow rate of 1.0ml/min. The detection was made at 235 nm. The retention times were 2.28min for [STS] and 3.14min for [NPS]. Calibration curve was linear over the concentration range of 125-750 µg/ml for [STS] and 20 to 120 µg/ml for [NPS]. The propose method was validated as per the ICH guidelines parameters like Linearity, specificity, precision, accuracy, robustness and ruggedness. The method was accurate, precise, specific and rapid found to be suitable for the quantitative analysis of the drug and dosage form.

KEY WORDS

Method development and validation, Naproxen, Tablets, C_{18} column, RP-HPLC.

1. INTORDUCTION

Naproxen sodium is 2-Napthaleneacetic acid, 6-methoxy-α-methyl-, sodium salt and Sumatriptan succinate 1H-Indole-5-methanesulfonamide,3-[2(dimethylamino)ethyl]-N-methyl-, butanedioate (1:1)[1]. NPS and STS are official in U.S. Pharmacopoeia [1].but there is no official method for the combination. Both drugs in combination of tablet dosage form in the ratio of 85:500 mg STS: NPS. As per literature survey many methods have been reported the estimation of STS and NPS individually or in combination with some other drugs[2-13]. With this present proposed method both STS and NPS estimates simple and economical in tablet formulation.

2. MATERIAL AND METHODS

2.1 Chromatographic Conditions

Waters e 2695 separation module with high pressure liquid chromatographic instrument provided with a Hypersil BDS C_{18} column (100 mm x 4.6 mm ; 5µ) and 2489 UV-Visible detector, auto injector, auto sampler with Empower 2 software from Waters corporation, Milford USA was employed in the study. HPLC grade acetonitrile, water were purchased from Ranbaxy, India, and Potassium dihydrogen phosphate, ortho phosphoric acid AR grade were purchased from SD Fine Chem Mumbai, India were used in the study.

2.2 Drug Samples

The reference samples were obtained from M/s. Bio-Leo Analytical Labs India Pvt Ltd, Hyderabad,

India, the formulation samples were purchased from local market.

2.3 Mobile phase

A mixture of phosphate buffer pH 6.5 and acetonitrile in the ratio 60:40 v/v was filtered through 0.22µ membrane filter and was degassed. Mobile phase was used as diluent for preparing the working solution of the drug. The mobile phase was filtered and sonicated by using Bio-Technics india, Mumbai before use. The flow rate of the mobile phase was maintained at 1ml/min. The column temperature was maintained at 30ºC and the detection of the drug was carried out at 235nm.

2.4 Preparation of stock and working standard solution of Sumatriptan and Naproxen

About 8.5mg of Sumatriptan succinate and 50 mg of Naproxen Sodium was weighed accurately on Sartorius semi micro balance model-CPA225D and transfers in to 50ml volumetric flask the solution was sonicated and the resulting solution was diluted with the mobile phase to get a working standard solution of 17 µg/ml STS AND 100 µg/ml NPS.

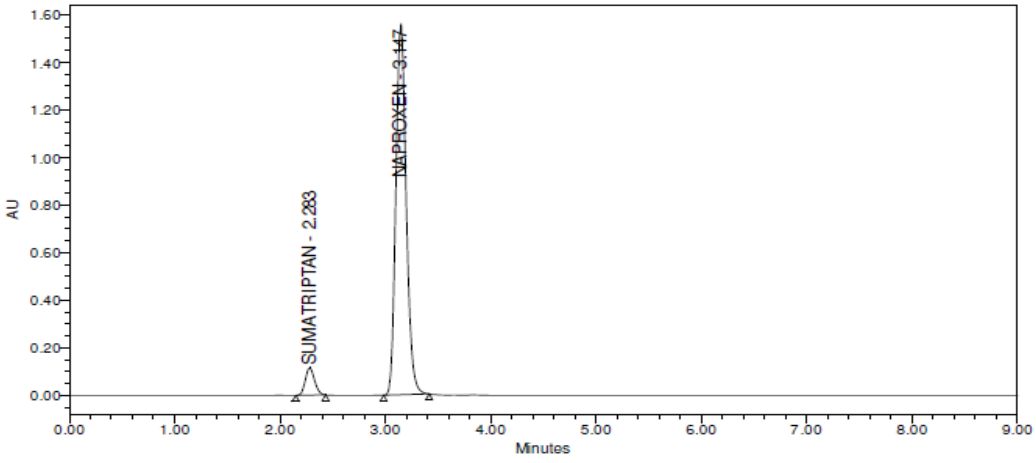
2.5 Sample Preparation

Weighed accurately previously weighed and crushed 20 tablets powder equivalent to 8.5mgof STS and 50 mg of NPS transferred to 50ml volumetric flask make up to the mark with mobile phase sonicated and filtered through whatman filter paper. Further dilute 10 ml to 100 ml with mobile phase.

2.6 Linearity and Construction of Calibration Curve

Linearity of the peak area response was determined by taking measurement at Six concentration prints (6 replicates at each point) working standard dilution of STS and NPS in the range of 4.25-25.5µg/ml and 25 to 150 µg/ml respectively. 20µl quantity of the dilution was injected each time in to the column. The drug elutes was monitored at 235 nm and the corresponding chromatograms were obtained. Form these chromatograms the mean peak areas were calculated and a plot of concentration over the peak area was constructed. This regression equation was later used to estimate the amount of STS and NPS in pharmaceutical dosage form. A representative chromatogram for the separation of STS and NPS presented in **Figure 1.**

Figure 1: Chromatogram of STS (17mcg/ml) & NPS (100mcg/ml)



	Peak Name	RT	Area	Height	% Area	Resolution	Symmetry Factor	USP Plate Count
1	SUMATRIPTAN	2.283	698154	114857	6.17		1.11	3197
2	NAPROXEN	3.147	10616250	1555163	93.83	5.13	1.16	4948

2.7 System Suitability Testing

The system suitability parameters such as Theoretical plates, tailing Factor and resolution were performed to verify the system is adequate for the analysis to be performed. The results are performed in **Table 1**.

Table 1: System suitability parameters

Parameters	Sumatriptan	Naproxen
Tailing Factor	1.11	1.16
Theoritical plates	3197	4948
Resolution	--	5.13
LOD(µg/ml)	0.5407	2.9543
LOQ(µg/ml)	1.6387	8.9526

RESULTS AND DISCUSSION

The present study was aimed at developing a simple economical precise and accurate HPLC method for the analysis of STS and NPS in bulk drug and in pharmaceutical dosage form. In order to achieve optimum separation of the component peaks, mixture of acetonitrile with water in different combinations were tested as mobile phase on a C_{18} stationary phase. A mixture of Phosphate buffer pH 6.5: acetonitrile in a proportion of 60:40 v/v was selected as the chromatographic peaks were well defined and resolved with no tailing. The retention time obtained for STS was 2.28±0.1 min and for NPS was 3.15±0.1min. Each of the samples was injected Six times and the Sample retention times were observed in all cases. The peak areas of STS and NPS were reproducible as indicated by low coefficient of variation. A good linear relationship

(r^2 = 0.999) was observed for STS and (r^2=0.999) was observed for NPS. The regression concentration and areas are given in **Table 2**. And the regression characters are given in **Figure 2 & 3**. When test solutions were analysed by the proposed method for finding out intra and inter-day variation, low co-efficient of variation was observed. The absence of additional peaks indicated non-interference of common excipients used in the tablets.

Table 2: Calibration data of the proposed method

Sumatriptan		Naproxen	
Conc (mcg/ml)	Mean Area	Conc (mcg/ml)	Mean Area
4.25	180282	25	2725561
8.5	356084	50	5454925
12.75	524727	75	8093281
17	701523	100	10742052
21.25	874029	125	13278587
25.5	1013140	150	15642564

Figure 2: Linearity of Sumatriptan

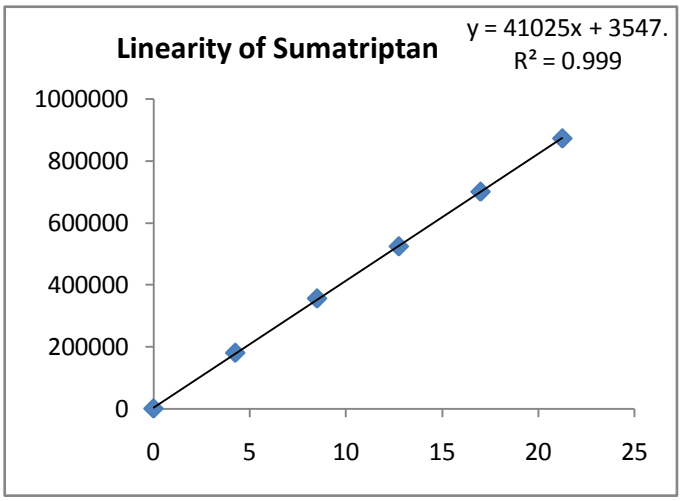


Figure 3: Linearity of Naproxen

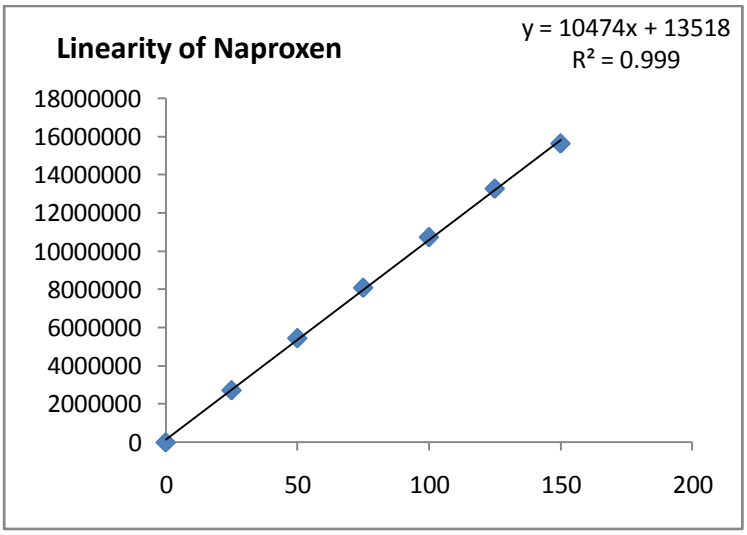


Table 3: Accuracy data (Triplicate values at 50,100 &150 percent levels)

	Amount added (µg)	Amount found (µg)	Percent Recovery	Percentage of mean recovery
Sumatriptan	8.5	8.487	99.85	99.85
	17.0	16.95	99.72	99.72
	25.5	25.31	99.27	99.27
Naproxen	50	49.85	99.69	99.69
	100	99.69	99.69	99.69
	150	149.88	99.92	99.92

*Each value is a mean of three readings

High recovery values obtained from the different dosage form by the proposed method indicates the method is accurate. The drug content in tablets was quantified using the proposed analytical method are given in **Table 3**.

The deliberate changes in the method have not much affected the peak tailing, Theoretical plates and the percent assay. This indicated the robustness of the method. The robustness study results are presented in **Table 4**. The lowest value of LOD and LOQ as obtained by the proposed method by calculated using 3.3xstdev/slope for LOD and 10xstdev/slpoe for LOQ. The standard solution of the drug was stable up to 24 hrs as the difference in percent assay during the above period is within limit system suitability parameters were studied with six replicates standard solution of the drug and the calculated parameters are within the acceptance criteria. The tailing factor and the number theoretical plate are in the acceptable limits.

Table 4: Robustness Study

Drug name	Variations	Chromatographic parameters				
		Retention time	Area	Height	Theoretical plates	Asymmetry
Sumatriptan	Buffer change ± 5%					
	55% v/v	2.021	689708	114346	3121	1.10
	60%v/v	2.284	698156	114687	3189	1.11
	65% v/v	2.588	697898	114598	3132	1.13
	Change in flow rate at ±0.1ml/min					
	1.flow rate at 0.90ml/min	2.485	697890	114646	3176	1.12
	2.flow rate at 1.0ml/min	2.262	696548	114536	3178	1.11
	3.flow rate at 1.10ml/min	2.050	695650	114502	3156	1.10
Naproxen	Buffer change ± 5%					
	55% v/v	2.845	10603245	1554657	4932	1.14
	60%v/v	2.275	10616250	1555163	4948	1.16
	65% v/v	3.487	10632446	1556324	4978	1.17
	Change in flow rate at ±0.10ml/min					
	1.flow rate at 0.90ml/min	3.478	10632560	1556032	4933	1.18
	2.flow rate at 1.0ml/min	2.284	10615467	1555098	4965	1.16
	3.flow rate at 1.10ml/min	2.769	10605454	1555002	4945	1.15

The system precision was established by six replicate injections of the standard solution containing analytes of interest. The values of relative standard deviation were found within the limit, indicating the injection repeatability of the method. The method precision was established by carrying out the analyte six times using the proposed method. The relative standard deviation was found within the limit, indicating the injection repeatability of the method.

The results were presented in **Table 5 & 6**.

The diluted preparations of marketed tablets were injected in duplicate and the results were calculated and presented in **Table 7**.

Table 5: Precision Study

Sumatriptan			Naproxen	
S.No.	**RT**	**Area**	**RT**	**Area**
1	2.283	684394	3.147	10631207
2	2.283	698154	3.147	10616250
3	2.283	692607	3.143	10621465
4	2.285	684783	3.145	10640231
5	2.284	698216	3.144	10617065
6	2.281	698547	3.146	10620674
Avg	2.283167	692783.5	3.145333	10624482
Stdev	0.001329	6723.022	0.001633	9376.966
%RSD	**0.06**	**0.97**	**0.05**	**0.09**

Table 6: Method Precision study

Sumatriptan			Naproxen	
S.No.	**RT**	**Area**	**RT**	**Area**
1	2.282	697205	3.144	10596700
2	2.282	698542	3.143	10607200
3	2.282	698316	3.141	10578197
4	2.284	696982	3.142	10589457
5	2.283	698782	3.145	10611543
6	2.282	698128	3.141	10565387
avg	2.2825	697992.5	3.142667	10591414
stdev	0.000837	733.422	0.001633	17539.9
%RSD	**0.04**	**0.11**	**0.05**	**0.17**

Table 7: Assay Results

Drug	Amount present/tablet	% of Assay
Sumatriptan	84.58 mg	99.51
Naproxen	499.75 mg	99.95

The specificity of the HPLC method was determined by the complete separation of STS and NPS. When it was subjected to forced degradation as per ICH guidelines which was carried out with 0.1N HCL, 0.1N NaOH and Heat degradation. The method does not permit detection of degradation product for STS and NPS.

Hence it can be concluded that the proposed HPLC method is evident very fast and economical compared to the literature available.

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