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SIMULTANEOUS ESTIMATION OF SUMATRIPTAN SUCCINATE AND NAPROXEN SODIUM BY REVERSE PHASE HPLC IN BULK AND PHARMACEUTICAL DOSAGE FORM

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ABSTRACT

This investigation describes a new precise, sensitive and accurate RP-HPLC method for the Simultaneous estimation of Sumatriptan succinate and Naproxen Sodium in Bulk and Tablets. The resolution of two drugs was achieved on XTerra C_{18} (150mm x 4.6mm i.d., 3.5µm particle size) column with UV detection at 284nm and the mobile phase consists of Buffer and Acetonitrile (25:75 v/v). Using chromatographic conditions described Sumatriptan succinate and Naproxen Sodium were well resolved with mean retention times of 2.622 and 4.070 min, respectively. Linear response (r>0.999) was observed over the range of 30-70µg/ml for Sumatriptan succinate and 20-60µg/ml for Naproxen Sodium. The lower limit of quantification and lower limit of detection was 10.02 and 3.0 for Sumatriptan succinate and 10.05 and 2.99 for Naproxen Sodium. The Validation parameters were performed according to the ICH guidelines and the proposed method can be useful in the routine analysis for the determination of Sumatriptan succinate and Naproxen Sodium in Pharmaceutical dosage forms.

INTRODUCTION: Sumatriptan [1-2] (SUM) (as the succinate), a selective 5-hydroxytryptamine1 receptor subtype agonist is chemically designated as 3-[2-(dimethylamino) ethyl]-N-methyl-indole-5-methane sulfonamide succinate (1:1). Naproxen sodium [3] (NAP) is a propionic acid derivative chemically designated as (S)-6-methoxy-a-methyl-2-naphthaleneacetic acid, sodium salt.

Both drugs in combination used in the treatment of migraine attacks. Literature survey reveals many methods for estimation of SUM [4-12] and NAP [13-17] individually and very few methods are available for simultaneous determination by UV [18-20], HPTLC [21] and HPLC [22-26].

In this communication, a new simple, rapid and precise HPLC method have been reported for simultaneous determination of SUM and NAP which can be used for its routine analysis in normal laboratories.

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MATERIALS AND METHODS: Chromatograms were made on Waters (Alliance) with Auto Sampler and Ultraviolet detector. The data acquisition was performed by Empower Software. Glass wares used in each step were rinsed thoroughly with double distilled water, dried in hot air oven.SUM and NAP was obtained from Pharma train institution, Hyderabad. The pharmaceutical preparation of combination of Sumatriptan succinate and Naproxen Sodium is SUMINAT PLUS (Unimed Technologies Ltd.India.) was obtained from local market. Acetonitrile used is HPLC grade obtained from MERCK (India) and water used is double distilled water. Other reagents were of AR grade.

Chromatographic Conditions: The used analytical column was XTerra C_{18} (150mm x 4.6mm i.d., 3.5µm particle size) column. The mobile phase consists of mixture of Buffer and Acetonitrile (25:75 v/v), filtered through 0.22µm Millipore filter and degassed by sonication. Separation was carried out isocratically, at ambient temperature (23±1°C), and a flow rate of 0.8 ml/min with Ultraviolet detection at 284nm.The injection volume was 20 µl.

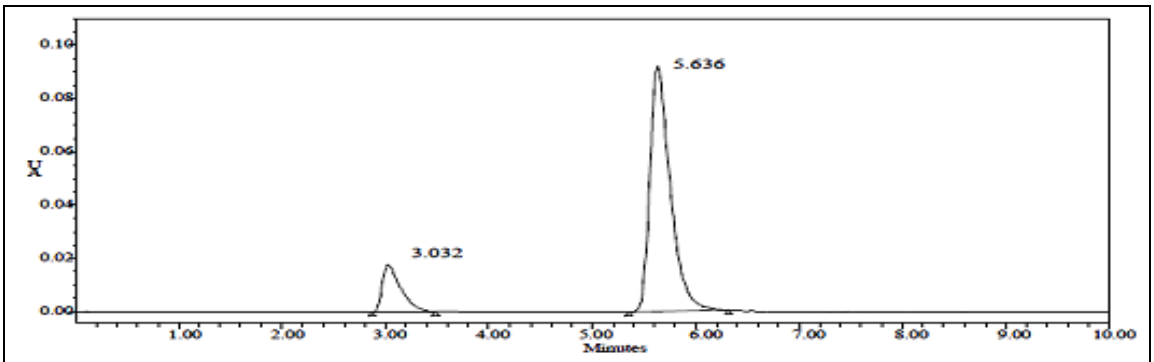
Preparation of Standard solutions: Accurately weigh and transfer 50 mg of SUM and 275 mg NAP into a 10mL clean dry volumetric flask. Add about 7mL of Diluent (Mobile phase) and sonicate to dissolve it completely and make volume up to the mark with the same solvent (Stock solution).Further pipette 1ml of SUM and NAP from the above stock solution into a 10ml volumetric flask and dilute up to the mark with diluent. Further pipette 1ml of SUM and NAP into a 10ml volumetric flask and dilute up to the mark with diluent.

Analysis of Marketed Formulation: Twenty tablets of SUM and NAP were crushed and made into powder. Accurately weigh and transfer equivalent to 50 mg of SUM and 275mg of NAP sample into a 10mL clean dry volumetric flask. Add about 7mL of Diluent and sonicate to dissolve it completely and make volume up to the mark with the same solvent (Stock solution). From this working standard of 32.5mg/ml was prepared. 20 µL of the standard, sample were injected into the chromatographic system and the areas were measured for the SUM and NAP peaks.

The content of SUM and NAP were calculated and found to be 100.2 and 100.1% respectively.

RESULT AND DISCUSSION:

Optimization of Chromatographic Conditions: Chromatographic conditions were optimized by changing the mobile phase composition and buffers used in the mobile phase. Different experiments were performed to optimize the mobile phase but adequate separation of drugs could not be achieved. By altering the pH of mobile phase a good separation was achieved. The optimized mobile phase consisting of 0.05 M Potassium dihydrogen Phosphate (pH 3.5 with Orthophosporic acid) and Acetonitrile mixed in the ratio of 25:75v/v and flow rate of 0.8 ml/min SUM and NAP were eluted at 3.032 and 5.636 minutes respectively with a run time of 10 min under the above optimized chromatographic conditions. Typical chromatograms for simultaneous estimation of SUM and NAP are shown in **Figure 1 & 2**.



	Name	Retention Time (min)	Area (µV*sec)	Height (µV)	USP Resolution	USP Plate Count	USP Tailing
1	Sumatriptan	3.032	215944	17808		2460.2	1.8
2	Naproxen	5.636	1271126	91884	7.2	3984.6	1.4

FIGURE 1: CHROMATOGRAM OF SUM AND NAP STANDARD

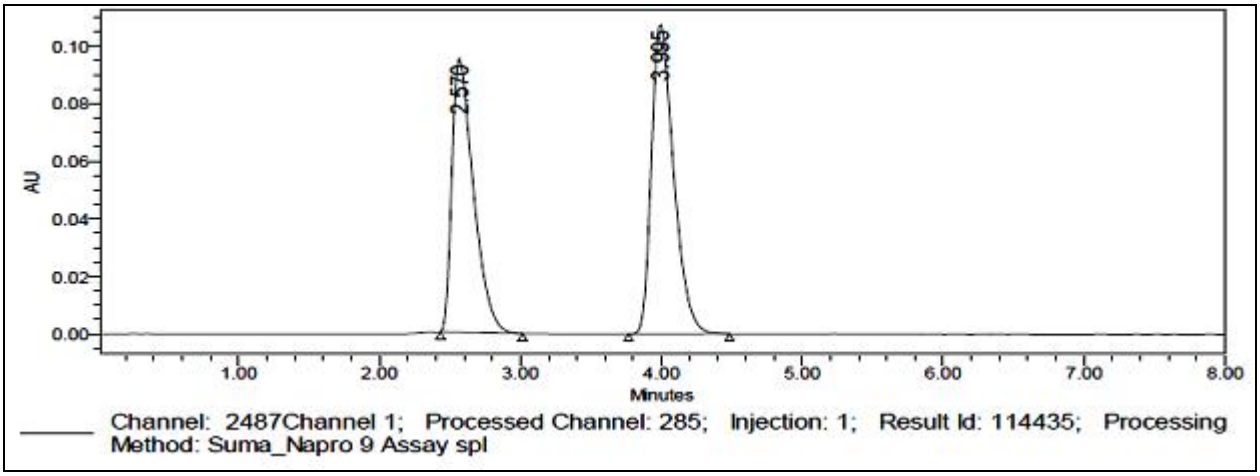


FIGURE 2: CHROMATOGRAM OF SUM AND NAP SAMPLE

Method Validation [27-28]:

System Suitability Results: For SUM and NAP peaks the tailing factor were found to be 1.8&1.4 respectively and the Theoretical Plates obtained were found to be 17808 & 91884 respectively.

Linearity: The calibration curves obtained by plotting Peak Area against Concentration for SUM and NAP. The linearity was obtained in the concentration range of 30-70 µg/ ml for SUM, and 20-60 µg/ml for NAP. The regression coefficient values (R^2) for SUM and NAP found to be 0.999 and 0.999 respectively.

Accuracy and Precision: The accuracy of the RP-HPLC method was determined by calculating Recoveries of SUM and NAP for 50%, 100% and 150% with respect to target concentration and results are tabulated in **Table 1 & 2** respectively. The System precision of the proposed method was determined by injecting standard solution for five times and measured the area for them in HPLC. The Method Precision of the proposed method was determined by injecting six sample solutions into HPLC prepared individually. The %RSD for the areas of system precision and method precision data were calculated and given in **Table 3**.

TABLE 1: RECOVERY RESULTS FOR SUM

%Concentration (at specification Level)	Area	Amount Added (mg)	Amount Found (mg)	Recovery %	Mean Recovery %
50%	111464	25.3	25.75	101.8	
100%	216811	50	50.1	100.2	100.1
150%	315761	74.2	72.96	98.3	

TABLE 2: RECOVERY RESULTS FOR NAP

%Concentration (at specification Level)	Area	Amount Added Found (mg)	Amount (mg)	Recovery %	Mean Recovery %
50%	646640	137.0	139.52	101.844	
100%	1270746	275	274.19	99.706	100.6
150%	1856662	400	400.6	100.154	

TABLE 3: PRECISION OF SUM AND NAP

S. No.	Precision	SUM	NAP
1.	System precision (Average Area and %R.S.D)	215705 and 0.08	1270312 and 0.01
2.	Method precision (Average Area and %R.S.D)	214874 and 0.033	1268940 and 0.034

Limits of Detection and Quantitation: For determining the limit of detection (LOD), 10mg of SUM and NAP was transferred in10mL clean dry volumetric flask add about 7mL of Diluent and sonicate to dissolve it completely and make volume up to the mark with the same solvent(Stock solution) separately. From this a working standard of 1µg/ml and0.8 µg/ml of SUM and NAP was prepared and injected separately. The LOD was found to be 3.0 for SUM and 2.99 for NAP.

For determining the limit of Quantitation, from the above stock solution, prepared 3.3µg/ml solution of SUM and 0.8µg/ml solution of NAP and injected. The LOQ was found to be 10.02 for SUM and 10.05 for NAP respectively.

Robustness: As part of the Robustness, deliberate change in the flow rate, mobile phase composition was made to evaluate the impact on the method. The results reveal that the method is robust enough. The results are summarized in **Table 4, 5, 6 and 7.**

TABLE 4: SYSTEM SUITABILITY RESULTS FOR SUM (FLOW RATE VARIED)

S. No	Flow Rate (ml/min)	System Suitability Results	
		USP Plate Count	USP Tailing
1	0.5	2126	1.4
2	0.6	2318	1.8
3	0.7	2011	1.3

TABLE 5: SYSTEM SUITABILITY RESULTS FOR NAP (FLOW RATE VARIED)

S. No	Flow Rate (ml/min)	System Suitability Results	
		USP Plate Count	USP Tailing
1	0.5	2395	1.2
2	0.6	3924.7	1.4
3	0.7	2311	1.2

TABLE 6: SYSTEM SUITABILITY RESULTS FOR SUM (MOBILE PHASE VARIED)

S. No.	Change in Organic Composition in the Mobile Phase	System Suitability Results	
		USP Plate Count	USP Tailing
1	10% less	2180	1.4
2	*Actual	2318	1.8
3	10% more	2051	1.4

TABLE 7: SYSTEM SUITABILITY RESULTS FOR NAP (MOBILE PHASE VARIED)

S. No.	Change in Organic Composition in the Mobile Phase	System Suitability Results	
		USP Plate Count	USP Tailing
1	10% less	2345	1.3
2	*Actual	3924.7	1.4
3	10% more	2235	1.2

***** Results for actual Mobile phase composition (Buffer and Acetonitrile (25:75 v/v)) have been considered from Accuracy standard

CONCLUSION: A new HPLC method was developed and validated for simultaneous determination of SUM and NAP in combined pharmaceutical dosage form and assured the satisfactory precision and accuracy and also determining lower concentration of each drug in its solid dosage form.

The method has been found to be better than previously reported methods, because of use of a less economical and readily available mobile phase, lack of extraction procedures, no internal standard, and use of the same mobile phase for washing of the column. All these factors make this method suitable for quantification of SUM and NAP in bulk drugs and in pharmaceutical dosage forms.

It can therefore be concluded that use of the method can save much time and money and it can be used in small laboratories with very high accuracy and a wide linear range.

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