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HPTLC METHOD FOR SIMULTANEOUS DETERMINATION OF NAPROXEN SODIUM AND SUMATRIPTAN SUCCINATE IN PHARMACEUTICAL DOSAGE FORM

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ABSTRACT

A rapid and simple high performance thin layer chromatography (HPTLC) method with densitometry at 230 nm was developed and validated for simultaneous determination of Naproxen sodium and Sumatriptan succinate from pharmaceutical preparation. Separation was performed on aluminum-backed silica gel 60F254 HPTLC plates as stationary phase and using a mobile phase comprising of methanol:distilled water:formic acid in the volume ratio of 0.5:7.5:0.1 (v/v/v), respectively. After development, plates were observed under UV light. The detector response was linear in the range of 200-1200 ng/spot and 100-1000 ng/spot for Naproxen sodium and Sumatriptan succinate. The validated lowest limit of detection was 85 ng/spot and 40 ng/spot whereas lowest limit of quantification was 200 ng/spot and 100 ng/spot for Naproxen sodium and Sumatriptan succinate, respectively. The percentage assay of Naproxen sodium and Sumatriptan succinate was found between 99.25 and 98.03 % respectively. The described method has the advantage of being rapid and easy. Hence it can be applied for routine quality control analysis of Naproxen sodium and Sumatriptan succinate from pharmaceutical preparation and stability studies.

INTRODUCTION: Naproxen (NAP) [1] is chemically 2- Naphthaleneacetic acid, 6 - methoxy -_- methyl -, (s) - (+) - (s) - 6- Methoxy -_- methyl- 2- naphthaleneacetic acid. Naproxen is a non-steroidal anti-inflammatory drug (NSAID) commonly used for the reduction of moderate to severe pain, fever, inflammation and stiffness. It works by inhibiting both the COX-1 and COX-2 enzymes. Like other NSAIDs, naproxen is capable of producing disturbances in the gastrointestinal tract. Sumatriptan succinate is a selective 5-hydroxytryptSUMAne1 receptor subtype agonist. Sumatriptan succinate [1-2] is chemically designated as 3- [2- (dimethylamino) ethyl]- N-methyl- indole- 5- methanesulfonamide succinate (1:1).

Sumatriptan succinate is official in European Pharmacopoeia and United State Pharmacopoeia suggests chromatographic method for sumatriptan succinate in bulk and tablet formulation. Several analytical techniques [3-12] like HPLC and LS-MS have been reported for sumatriptan succinate in combination with other drugs. However, no references are reported so far for the simultaneous determination of both drugs in combined dosage form or any such pharmaceutical preparations by HPTLC. In this communication we report a new simple, rapid and precise HPTLC method for simultaneous determination Naproxen- sodium and Sumatriptan succinate in combination capsule, which can be used for its routine analysis in ordinary laboratories.

MATRERIALS AND METHOD:

Chemicals and reagents: The Naproxen sodium and Sumatriptan succinate working standards were obtained as a gift sample from Sun Pharmaceuticals Ltd. Vadodara, Gujarat. The formulation, tablet with combination of Naproxen sodium 500 mg and Sumatriptan succinate 80 mg is available in market by brand name TREXIMET; methanol and formic acid were of Qualigens; pre-coated silica gel 60 F254 HPTLC plates (Merck # 5548) of E-Merck**.** All dilutions were performed in standard volumetric flasks.

Instrumentation and chromatographic conditions: Chromatography was performed on pre-coated silica gel 60 F254 HPTLC plates (Merck# 5548). Before use they were pre-washed with methanol and dried in an oven at 105^{o}C for 2 h. 10 µL of sample were spotted 8 mm from the edge of the plates by means of a Camag Linomat IV sample applicator. The plates were developed to a distance of 85mm in a Camag twin-trough chamber previously equilibrated 15min with mobile phase *i.e*. methanol, distilled water, Formic acid in the volume ratio of 0.5:7.5:0.1 (*v/v*) methanol: distilled water: formic acid. The chromatographic conditions had previously been optimized to achieve the best resolution and peak shape. Plates were evaluated by densitometry at Lambda max 230 nm with a Camag Scanner II, in conjunction with CATS software for quantitation. The typical chromatogram is shown **Figure 1.**

Preparation of standard stock solution of Naproxen sodium: Accurately weigh 10 mg pure standard of Naproxen sodium and transfer to 10 mL volumetric flask. The drug was dissolved in distilled water, diluted up to the mark with distilled water and mixed well. This gave a standard stock solution of strength 1000 µg/mL of Naproxen sodium.

Preparation of standard stock solution of Sumatriptan succinate: Accurately weigh 10.0 mg pure standard of Sumatriptan succinate and transfer to 10mL volumetric flask. The drug was dissolved in distilled water, diluted up to the mark with distilled water and mixed well. This gave a standard stock solution of strength 1000 µg/mL of Sumatriptan succinate.

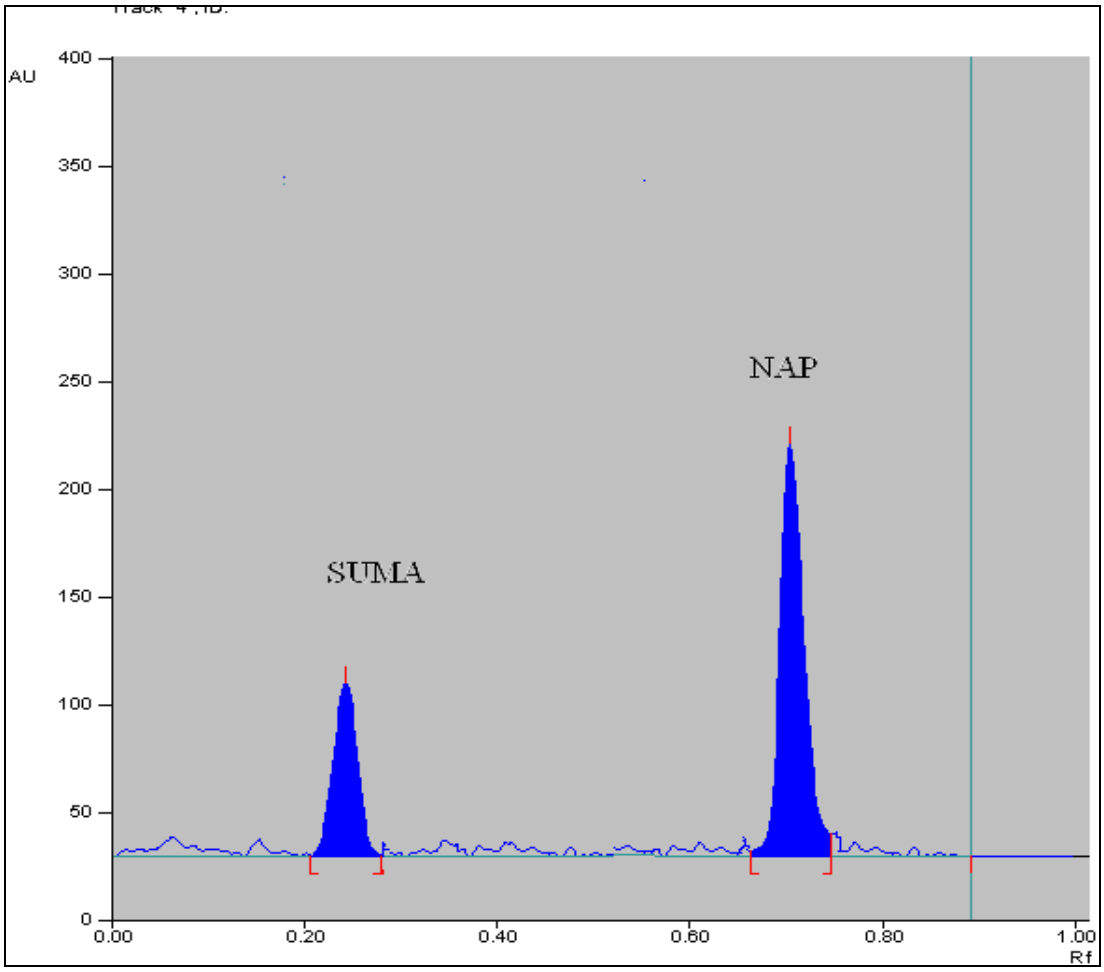

FIG. 1: HPTLC CHROMATOGRAM OF NAP AND SUMA

Preparation of sample solution: Twenty tablets (TREXIMET) were weighed and the average weight was calculated. The tablets were crushed to furnish a homogeneous powder and a quantity equivalent to one tablet was weighed in a 100 mL standard volumetric flask. The powder dissolved in distilled water and diluted up to the mark with distilled water. That solution was then sonicated for 30 min. Then cooled to room temperature and diluted with distilled water. The solution was filtered through Whatmann No. 41 filter paper and the filtrate was used as sample solution.

Validation Procedures:

Linearity: Seven different concentrations of mixture of Naproxen sodium, Sumatriptan succinate were prepared from stock solution of Naproxen sodium (1000 µg/mL) and Sumatriptan succinate (1000 µg/mL) in the range of 200-1200 ng/spot and 100-1000 ng/spot respectively, in distill water to obtain desire linearity range. The detector response to the different concentrations was measured. The drug peak-area was calculated for each concentration level and a graph was plotted of drug concentration against the peak area. This experiment was carried out thrice and the mean peak area response was used for the calculations. The data were analyzed by linear regression least-squares fitting. The statistical data obtained are given in **Table 1**.

Limit of detection and limit of quantitation: The limit of detection (LOD) was found to be 85 ng/spot for Naproxen sodium and 40 ng/spot for Sumatriptan succinate. Limit of quantitation (LOQ) for Naproxen sodium and Sumatriptan succinate were determined experimentally by spotting six replicates of each drug at LOQ concentration. The LOQ of Naproxen sodium and Sumatriptan succinate were found to be 200 ng/spot and 100.0 ng/spot respectively.

System suitability: A system- suitability experiment was performed before determination of Naproxen sodium and Sumatriptan succinate in unknown samples. The coefficient of variation (CV) for peak area and Rf value for both the drugs was less than 2.0% for six replicates measurement of the same sample. This shows that the method and the system are suitable for determination of Naproxen sodium and Sumatriptan succinate.

Assay (from the pharmaceutical preparation): 10 µL working standard solution and sample solutions were spotted on the plate and the plate was developed and evaluated as described above. The procedure was repeated five times, individually weighing the tablet powder each time. The densitometric responses from the standard and sample were used to calculate the amounts of the drug in the tablet. The results obtained are as shown in **Table 2.**

TABLE 1: SUMMARY OF VALIDATION PARAMETERS OF PROPOSED HPTLC METHOD

Parameters	NAP	SUMA
Range (ng/spot)	200-1200	100-1000
Regression equation y=mx+c	Y=1035.89X+ (-1123.61)	Y= 5314.14X+ (-1860.85)
Slope	1035.89	5314.14
Intercept	1123.61	1860.8
Correlation coefficient (r^2)	0.9973	0.9945
LOD (ng per spot)	85.0	40.0
LOQ (ng per spot)	200.0	100.0
%Recovery ± SD,(n=3)	100.36± 0.21 %	100.27 ± 0.91
Repeatability (%RSD, n=6),	0.13	0.86
Interday precision (%RSD) (n = 3) at 3 range	0.41-0.61	0.12-0.31
Intraday precision (%RSD) (n = 3) at 3 range	0.60-0.89	0.28-0.63

[a]SD = Standard deviation, [b]RSD = Relative standard deviation

TABLE 2: ANALYSIS OF NAP AND SUMA IN FORMULATIONS BY PROPOSED METHOD (N=6)

Formulation	Label Amount (mg)		Amount found (mg)		% Assay ± SD	
	NAP	SUMA	NAP	SUMA	NAP	SUMA
Tablet	80	500	79.40	490.15	99.25 ± 0.16	98.03 ± 0.10

Recovery studies: The accuracy of the experiment was established by spiking pre-analyzed sample with known amounts of the corresponding drugs at three different concentration levels i.e. 20, 40 and 60 % of the drug in the tablet (the external standard addition technique). The spiked samples were then analyzed for five times. The results from recovery analysis are given in Table 1 the mean recovery is within acceptable limits, indicating the method are accurate.

RESULTS AND DISCUSSION: Use of pre-coated silica gel HPTLC plates with methanol, distilled water, Formic acid in the volume ratio of 0.5:7.5:0.1 (v/v) resulted in good separation of the drugs. Figure 1 show a typical densitogram obtained from Naproxen sodium and Sumatriptan succinate. Regression analysis of the calibration data for Naproxen sodium and Sumatriptan succinate showed that the dependent variable (peak area) and the independent variable (concentration) were represented by the equations Y=1035.89X+ (-1123.61) for Naproxen sodium and Y= 5314.14X+ (-1860.85) for Sumatriptan succinate. The correlation of coefficient (r2) obtained was 0.9973 for Naproxen sodium and that for Sumatriptan succinate is 0.9945. That means a good linear relationship was observed between the concentration range 200-1200 ng/spot and 100-1000 ng/spot for Naproxen sodium and Sumatriptan succinate, respectively.

The system suitability experiment was carried out before the determination of Naproxen sodium and Sumatriptan succinate in unknown samples. The coefficient of variation was less than 2% for replicate measurements of the same sample. This shows that the method and the system both are suitable for the determination of unknown samples. The assay of Naproxen sodium and Sumatriptan succinate was found to be 99.25 and 98.03 %. From the recovery studies it was found that about 100.36% and 100.27% of Naproxen sodium and Sumatriptan succinate respectively which indicates high accuracy of the method. The absence of additional peaks in chromatogram indicates non- interference of the common excipients used in tablets.

CONCLUSION: As the proposed method is highly accurate, selective and precise hence can be used for a routine quality-control analysis and quantitative simultaneous determination of Naproxen sodium and Sumatriptan succinate in pharmaceutical preparations. The method is also fast and requires approximately 40 min for analysis.

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