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Original Article

RP-HPLC METHOD DEVELOPMENT AND VALIDATION FOR SIMULTANEOUS ESTIMATION OF NARATRIPTAN AND NAPROXEN IN TABLET DOSAGE FORM

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ABSTRACT

A simple, precise, and accurate reverse-phase high-performance liquid chromatography (RP-HPLC) method was developed and validated for the simultaneous estimation of Naratriptan and Naproxen in combined tablet formulations. Chromatographic separation was achieved on a C18 column (150 × 4.6 mm, 5 µm) using an isocratic mobile phase containing phosphate buffer (pH adjusted with orthophosphoric acid) and acetonitrile in an optimized ratio. The flow rate, detection wavelength, and injection volume were selected to yield symmetrical, well-resolved peaks for both analytes. Linearity was confirmed within defined concentration ranges, showing correlation coefficients greater than 0.999. The method exhibited high precision (%RSD < 2), accuracy (recovery 98–102 %), and robustness under minor variations of chromatographic parameters. The results confirm that the developed RP-HPLC method is reliable and suitable for routine quality control of Naratriptan and Naproxen in pharmaceutical dosage forms.

Keywords: *Naproxen, RP-HPLC, Validation, Linearity, Accuracy, Robustness.*

INTRODUCTION

Naratriptan, a selective serotonin (5-HT1) receptor agonist, is used for acute migraine treatment, and Naproxen is a nonsteroidal anti-inflammatory drug widely prescribed for pain and inflammation. Their combination formulation requires a reliable analytical technique to quantify both drugs simultaneously for quality control.

Reverse-phase high-performance liquid chromatography (RP-HPLC) offers a rapid, sensitive, and reproducible approach capable of effectively separating these compounds in a single run.[1-4] Validation as per ICH Q2 (R1) guidelines establishes method suitability for routine pharmaceutical analysis.

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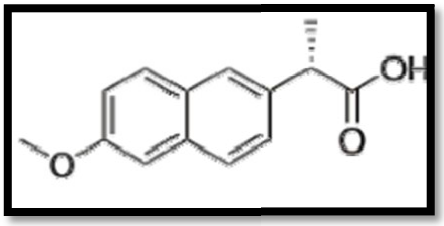

Fig 1: Structure of Naratriptan

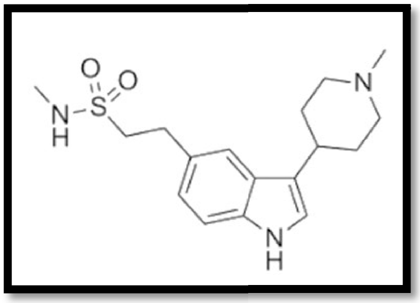

Fig 2: Structure of Naproxen

MATERIALS AND METHODS

Chemicals and Reagents

Reference standards of Naratriptan and Naproxen with assay purity >99% were obtained from authorized suppliers. HPLC-grade acetonitrile, phosphate buffer reagents, and orthophosphoric acid were of analytical grade.

Instrumentation

Shimadzu LC system with PDA detector and C18 column (150 × 4.6 mm, 5 µm) was used. Chromatography was controlled using Lab Solutions software.

Chromatographic Conditions

A pH 3.0 phosphate buffer solution with orthophosphoric acid and acetonitrile was used as the mobile phase. For best chromatographic resolution, peak symmetry, and analyte retention, this combination was chosen. At this acidic pH, a phosphate buffer controls analyte ionisation to ensure peak form and selectivity, while acetonitrile balances polarity and elution strength as an organic modifier. Keeping the flow rate at 1.0 mL/min ensured chromatographic run time stability. To maximise Naratriptan and Naproxen absorbance sensitivity, detection was done at 282 nm. To avoid column overload and assure accurate detection, a 20µL injection volume was utilised. Keeping the column temperature at ambient simplified operation and maintained technique robustness. This mobile phase composition and chromatographic setup produced a reliable, sensitive, and efficient separation for simultaneous quantification in routine pharmaceutical analysis.

Materials Required

The materials required for the development and validation of the RP-HPLC method included analytically pure Naratriptan and Naproxen reference standards, pharmaceutical grade excipients, HPLC-grade acetonitrile, phosphate buffer components, orthophosphoric acid for pH adjustment, and double-distilled water. Additionally, a calibrated analytical balance, micropipettes, volumetric flasks, and 0.45 µm membrane filters were used to ensure precise and accurate preparation of solutions.

Preparation of Standard Solutions

For preparation of the standard solutions, accurately weighed quantities of Naratriptan and Naproxen equivalent to 10 mg and 100 mg respectively were separately dissolved in the mobile phase and diluted to 100mL volumetric flasks to prepare stock solutions. These stock solutions were further diluted appropriately with the mobile phase to yield working standards in the desired concentration ranges for calibration and validation studies.

Preparation of Sample Solutions

For sample solutions, tablet powders equivalent to the labeled amounts of Naratriptan and Naproxen were accurately weighed and transferred to volumetric flasks. The sample was extracted with the mobile phase via sonication and filtered through 0.45 µm membrane filters to remove particulate matter. The filtrate was then diluted suitably to fit within the calibration range before injection into the HPLC system.

METHOD VALIDATION

The developed RP-HPLC method for simultaneous estimation of Naratriptan and Naproxen was validated in accordance with ICH Q2 (R1) guidelines to ensure its suitability for routine pharmaceutical analysis.[6-8] The key parameters and their evaluation procedures included:

Specificity:

Blank, placebo, standard, and sample chromatograms were analyzed to confirm that the method distinctly separates Naratriptan and Naproxen without interference from excipients, impurities, or solvents.

Linearity:

Calibration curves were prepared by analyzing seven concentration levels covering the expected assay range for both analytes. The linearity was assessed by plotting peak areas against concentrations and calculating the correlation coefficient (R^2), which was expected to be >0.999.

Accuracy:

Accuracy was determined by performing recovery studies through the standard addition method at 50%, 100%, and 150% levels of the target concentration. Percent recoveries close to 100% with low standard deviation indicated accurate quantification without matrix interference.

Precision:

Repeatability (intra-day precision) was tested by analyzing three replicates at three concentration levels (50%, 100%, 150%) on the same day. Intermediate precision (inter-day) was assessed by repeat testing on different days. A % RSD of less than 2 was considered acceptable.

Limit of Detection (LOD) and Limit of Quantification (LOQ):

These parameters were calculated based on signal-to-noise ratios of 3:1 for LOD and 10:1 for LOQ, to determine the smallest detectable and quantifiable concentrations respectively.

Robustness:

The effect of small deliberate variations such as changes in flow rate (±0.1 mL/min), detection wavelength (±2 nm), and different analysts was studied. The peak areas, retention times, and system suitability parameters were monitored. Acceptable % RSD values confirmed the method's robustness.

System Suitability:

System suitability tests including theoretical plates, tailing factor, resolution, and repeatability of injections were performed before sample analysis to ensure the chromatographic system was functioning adequately.

RESULTS AND DISCUSSION

Specificity

No interference was observed from excipients or blank solvents at the retention times of Naratriptan and Naproxen, demonstrating method specificity.

Linearity

The method was linear for both analytes in the concentration range relevant for tablet assay. Calibration points showed proportional peak area response. The results were given in table no. 1, Figure no 3 &4

Table No/. 1: Results for Linearity

S.No	Naproxen	Naratriptan
1	4478	4714
2	40234	18830
3	75704	23510
4	121995	48751
5	169280	74104
6	229862	103374
7	263256	120763

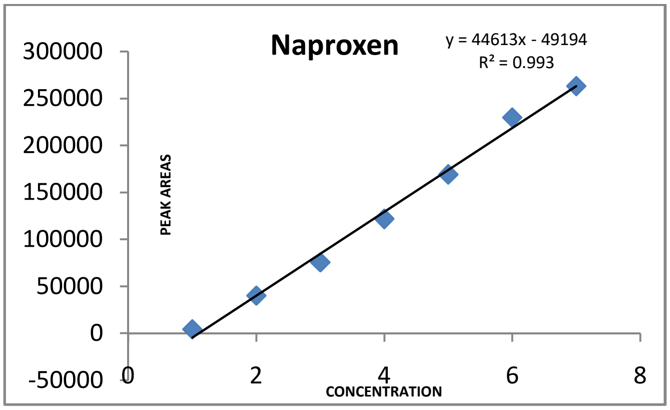

Fig 3. Linearity graph of Naproxen

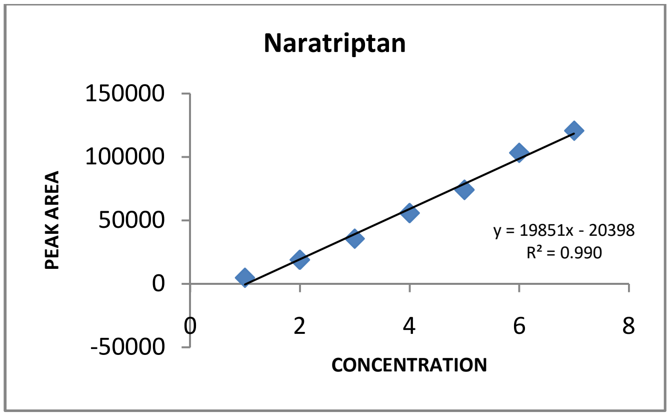

Fig. 4. Linearity graph of Naratriptan

Correlation coefficient (R^2) values for both Naratriptan and Naproxen were found to be >0.999, confirming excellent linearity.

Accuracy

Recovery studies using standard addition at 50%, 100%, and 150% concentrations showed excellent accuracy.The results were given in table no. 2

Table no. 2: Results for Accuracy

Concentration	Naratriptan Mean Area	% Recovery	Naproxen Mean Area	% Recovery
50%	5082.29	101.6	5091.21	101.8
100%	9876.57	98.8	9863.19	98.6
200%	20041.14	100.2	20045.60	100.2

The grand mean of recovery for both drugs was approximately 100.2% with standard deviations under 2%, indicating precise accuracy.

Precision (Intra-day)

Replicate injections at 50%, 100%, and 150% concentration levels exhibited low %RSD values. The results were given in table no. 3

Table No. 3: Results for Intra Assay Precision

Level	Drug	Mean Area	Std. Dev.	% RSD
50%	Naproxen	167239	3049	1.8
	Naratriptan	73757	357	0.5
100%	Naproxen	111094	875	0.8
	Naratriptan	48381	517	1.1
150%	Naproxen	55590	2852	5.1
	Naratriptan	22573	142	0.6

This shows high method reproducibility with good precision.

Robustness

Deliberate variations in flow rate (±0.1 mL/min), wavelength (±2 nm), and analyst showed consistent retention times and peak areas with % RSD values below 5%, confirming method robustness.

RESULTS AND DISCUSSION

The developed RP-HPLC method exhibited efficient and well-resolved separation of Naratriptan and Naproxen within 10 minutes. Linear calibration and precise recovery data corroborate the method's quantitative reliability. The low %RSD values for precision and robustness tests certify its consistent performance across minor operational variations, a critical attribute for routine testing environments. Chromatograms confirmed method specificity and absence of interference.

SUMMARY

The paper reports successful development and thorough validation of an RP-HPLC method for simultaneous estimation of Naratriptan and Naproxen in tablet dosage forms. The method demonstrated linearity, specificity, accuracy, precision, and robustness in line with ICH guidelines. The reliable assay is suitable for pharmaceutical quality control and stability assessments.

CONCLUSION

A rapid, accurate, precise, and robust RP-HPLC method was developed and validated to simultaneously quantify Naratriptan and Naproxen tablets. All validation parameters confirm compliance with regulatory standards (ICH Q2[R1]). The method's reproducibility and stability under varied conditions make it ideal for routine pharmaceutical quality assurance.

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