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RP-HPLC METHOD FOR SIMULTANEOUS ESTIMATION OF SUMATRIPTAN SUCCINATE, NAPROXEN SODIUM AND DOMPERIDONE

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ABSTRACT

A simple, accurate and precise RP-HPLC method was developed for the Simultaneous estimation of Sumatriptan Succinate, Naproxen Sodium and Domperidone in bulk as well as tablet dosage form. The chromatography was performed using a C-18 column. Eluents were monitored by UV detection at 280 nm and the mobile phase used was Acetonitrile: Methanol: 20mM Phosphate Buffer pH 4 (10:50:40). Sumatriptan Succinate, Domperidone and Naproxen Sodium showed a retention time of 1.64, 3.83 and 7.53 minutes respectively. The method was statistically validated for linearity, accuracy, precision. The linearity was within the concentration range of 3.125-37.5 µg/ml, 31.25-375 µg/ml and 1.25-15 µg/ml for Sumatriptan Succinate, Naproxen Sodium and Domperidone respectively. The limits of detection (LOD) were 0.75 µg/ml, 8.26 µg/ml and 0.27 µg/ml and limits of quantitation (LOQ) were 2.27 µg/ml, 25.05 µg/ml and 0.83 µg/ml for Sumatriptan Succinate, Naproxen Sodium and Domperidone respectively.

KEYWORDS: Sumatriptan Succinate, Naproxen Sodium, Domperidone, RP-HPLC, Migraine.

INTRODUCTION

Migraine.[1-3] is a chronic neurovascular disorder characterized by recurrent attacks of often severe headache, typically presenting with nausea and sensitivity to light and/or sound. In adults, migraine attacks usually last from 4 to 72 hours. Migraine headache is typically throbbing, unilateral, and aggravated by physical activity. There are two major subtypes of migraine: migraine without aura (also called common migraine) and migraine with aura (also

called classic migraine). Migraine with aura is characterized by focal neurological symptoms that typically precede, or sometimes accompany, the headache. These focal neurological symptoms are absent in migraine without aura. Some patients may present with both subtypes of migraine. Drug therapy of migraine has to be individualized based on severity and frequency of attacks and response of individual patient to various drugs. Currently the most common drugs in the treatment of attacks can be categorized into two main groups i.e. non-migraine specific drugs (antiemetics, simple analgesics, non-steroidal anti-inflammatory drugs (NSAID), combined analgesics, opiods) and migraine-specific drugs (ergot derivatives and triptans). Among these Sumatriptan succinate, Naproxen sodium and Domperidone are widely used.[1,4,5]

Literature survey revealed a number of methods for the estimation of Sumatriptan Succinate, Naproxen Sodium and Domperidone by means of various analytical techniques like LC-MS/MS, RP-HPLC, UV spectrophotometry and electrochemical methods either individually or as two drug combinations.[5-14]

In the present study an attempt was made to include an antiemetic drug, Domperidone with Sumatriptan Succinate and Naproxen Sodium as antimigraine therapy suggests the management of pain and emesis. Hence the study describes the development and validation of RP-HPLC method for simultaneous estimation of Sumatriptan Succinate, Naproxen Sodium and Domperidone in bulk and pharmaceutical dosage forms.

MATERIALS AND METHOD

Drugs and Chemicals

Sumatriptan Succinate was procured from Vergo Pharma, Verna- Goa, Naproxen Sodium from Marksans Pharma, Verna- Goa and Domperidone from Wallace Pharmaceuticals, Bethora Ponda -Goa as gift samples. HPLC grade Methanol, Acetonitrile and Water were procured from Merck Specialties private ltd. All other reagents used for the analysis were analytical grade.

Preparation of Standard Stock Solutions

12.5 mg of Sumatriptan Succinate, 125mg of Naproxen Sodium and 5mg of Domperidone were accurately weighed and transferred to a 100ml volumetric flask and dissolved in the mobile phase to obtain a final concentration of 125 µg/ml, 1250 µg/ml and 50 µg/ml for

Sumatriptan Succinate, Naproxen Sodium and Domperidone respectively. Aliquots of this solution were further diluted with the same to obtain final concentrations.

Preparation of Sample solution

Oro-dispersible tablets containing 25mg, 250mg and 10mg of Sumatriptan Succinate, Naproxen Sodium and Domperidone respectively were formulated in-house and were used for the analysis. Twenty tablets were weighed and their average weight was determined. The tablets were then crushed and their contents were mixed thoroughly. A portion of powder equivalent to 12.5 mg of Sumatriptan Succinate, 125mg of Naproxen Sodium and 5mg of Domperidone was accurately weighed and transferred to a 100ml volumetric flask and 70ml mobile phase was added. This was shaken for 2 minutes and then sonicated for 15 minutes, the volume was made upto the 100ml mark with mobile phase and the resulting solution was shaken for 1 minute. This solution was filtered using 0.45µm membrane filter using a vacuum filter assembly to remove any insoluble matter. 1ml of the filtered solution was transferred to a 10ml volumetric flask and the volume was made up using the mobile phase to obtain a working sample concentration of 12.5 µg/ml, 125 µg/ml and 5 µg/ml for Sumatriptan Succinate, Naproxen Sodium and Domperidone respectively.

Chromatographic Conditions

The method was developed using RP-HPLC technique. Sumatriptan Succinate, Naproxen Sodium and Domperidone were eluted in isocratic mode with a flow rate of 1.0ml/min using a mobile phase consisting of 20mM Phospahate Buffer pH 4:Methanol:Acetonitrile in the ratio of 40:50:10. The wavelength of the UV-Vis detector was set to 280nm. Grace^{TM} PN GEN-5 C18 5µm (4.6 x 150 mm) column was used. The column was thermostated at 25^0c.

Method Validation

The RPHPLC method was validated as per ICH guidelines Q2 (R1) evaluating for linearity, precision, accuracy and robustness.[15]

Linearity

Solutions were prepared in triplicate at concentrations of 3.125, 6.250, 9.375, 12.500, 15.625, 18.750, 21.875, 25.000, 37.5 µg/ml for Sumatriptan Succinate, 31.25, 62.50, 93.75, 125.00, 156.25, 187.50, 218.75, 250.00, 375.00 µg/ml for Naproxen Sodium and 1.25, 2.50, 3.75, 5.00, 6.25, 7.50, 8.75, 10.00, 15 µg/ml for Domperidone. Standard plot was constructed and

linearity was evaluated statistically by linear regression analysis that was calculated by least-squares regression.

LOD and LOQ

The LOD and LOQ values were not determined experimentally, the values were calculated from the Calibration curve of the three drugs.

Precision (Analysis of Tablet dosage form)

The precision of the method was determined by repeatability. Six sample solutions of tablet dosage form were prepared at 12.5 µg/ml, 125 µg/ml and 5 µg/ml for Sumatriptan Succinate, Naproxen Sodium and Domperidone respectively. The results were expressed as % RSD. The assay was performed and content per tablet were calculated.

Accuracy

To study the accuracy of the method recovery experiments were carried out. The accuracy of the test method was determined by preparing recovery samples (Spiking method) at the level of 80%, 100% and 120% of the targeted test concentration i.e. (12.5 µg/ml, 125 µg/ml and 5 µg/ml for Sumatriptan Succinate, Naproxen Sodium and Domperidone respectively). The results were expressed as the percentage of Sumatriptan Succinate, Naproxen Sodium and Domperidone reference standard recovered from the sample. All solutions were prepared in triplicate and assayed.

Robustness

Robustness testing was performed to evaluate the susceptibility of measurements under deliberate variations in the in the selected analytical conditions. Flow rate was varied by $\pm$ 0.1 ml/min, pH by $\pm$ 0.1 pH unit and Column thermostat temperature by $\pm 2^{O}C$.

RESULTS AND DISCUSSION

The goal of the study was to develop rapid RP-HPLC method for the analysis of Sumatriptan Succinate, Naproxen Sodium and Domperidone in bulk as well as in formulations using the most commonly employed C18 column with UV detection at appropriate wavelength. Sumatriptan Succinate, Domperidone and Naproxen Sodium showed a retention time of 1.64, 3.83 and 7.53 minutes respectively. The representative chromatogram indicating Sumatriptan Succinate, Naproxen Sodium and Domperidone is shown in figure 1.

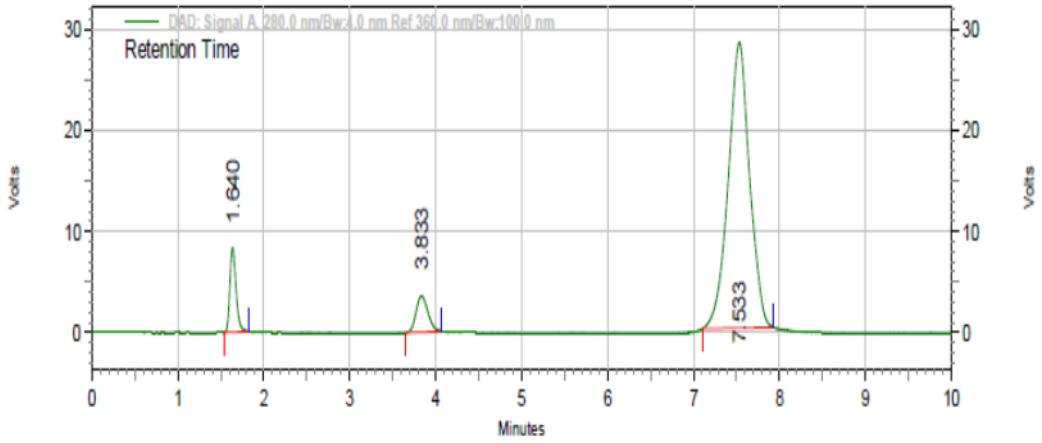
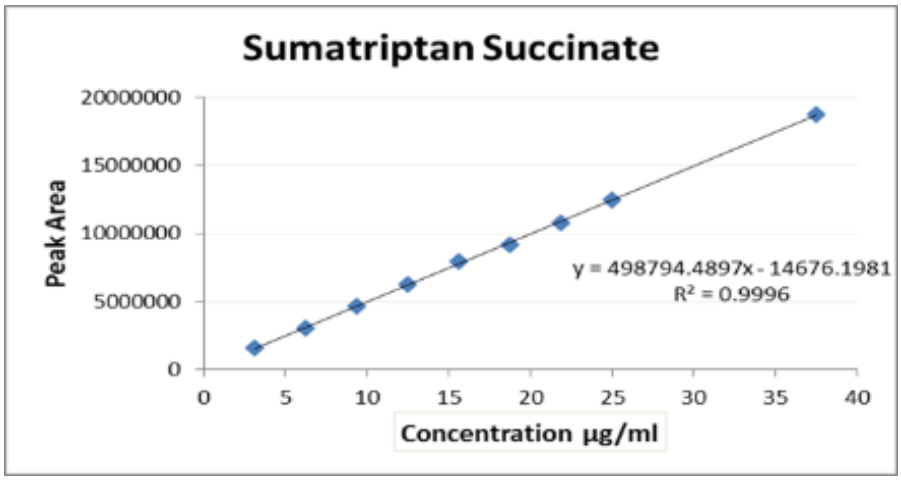
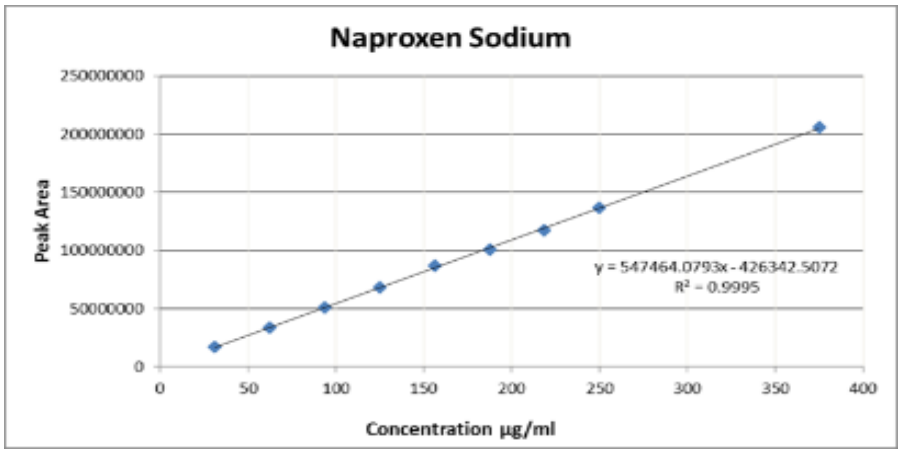


Figure 1: Chromatogram of Sumatriptan Succinate (1.64min), Domperidone (3.83min) and Naproxen Sodium (7.53min)

Linearity and Range

A good linear relation was found between the concentration and area for Sumatriptan Succinate, Naproxen Sodium and Domperidone. Calibration curves for Sumatriptan Succinate, Naproxen Sodium and Domperidone were constructed by plotting area versus the concentration which showed good linearity in the range of 3.125-37.5 µg/ml, 31.25-375 µg/ml and 1.25-15µg/ml for Sumatriptan Succinate, Naproxen Sodium and Domperidone respectively as indicated in figures The trend line equation obtained was y=498794.4897x-14676.1981, y=547464.0793x-426342.5072, y=1089573.1372x-56802.7295 and the regression coefficient was 0.9996, 0.9995, 0.9997 for Sumatriptan succinate, Naproxen sodium and Domperidone respectively.





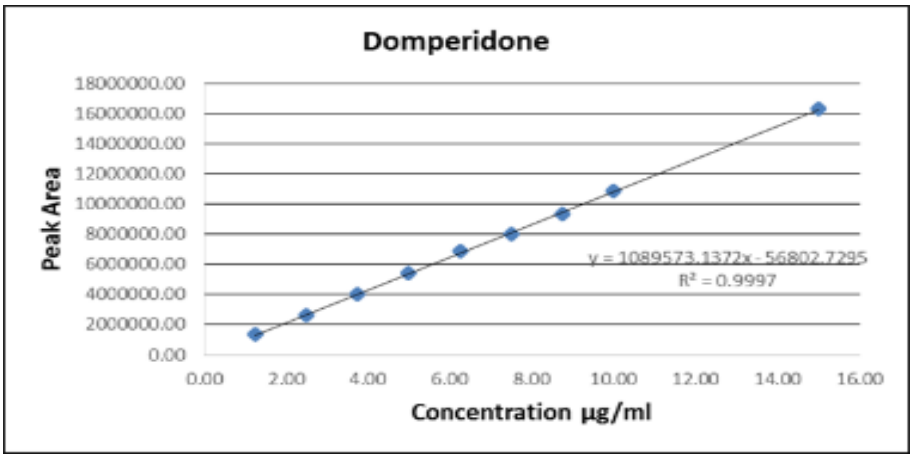


Fig 2: Calibration curve of Sumatriptan Succinate, Naproxen Sodium and Domperidone

Table 1: The values of LOD and LOQ

	Sumatriptan Succinate	Naproxen Sodium	Domperidone
LOD	0.75 µg/ml	8.26 µg/ml	0.27 µg/ml
LOQ	2.27 µg/ml	25.05 µg/ml	0.83 µg/ml

Accuracy

The mean % recovery for Sumatriptan Succinate was found to be between 100.172-100.73%, for Naproxen Sodium between 100.01-100.64% and Domperidone between 99.84-100.59%. The results are tabulated in Table 2.

Table 2: Accuracy Data

Amount of Standard added µg/ml	Amount Recovered µg/ml*	% Recovery*
Sumatriptan Succinate 3.75 6.25 8.75	 3.756 6.296 8.768	 100.172 100.737 100.212
Naproxen Sodium 37.5 62.5 87.5	 37.66 62.90 87.60	 100.436 100.641 100.012
Domperidone 1.5 2.5 3.5	 1.508 2.511 3.484	 100.594 100.545 99.841

*Mean of three readings.

Precision

The method showed insignificant variation in results i.e. the %RSD of assay was found to be 0.54%, 0.375% and 0.731% for Sumatriptan succinate, Naproxen sodium and Domperidone respectively which was well within the acceptance limit of 2%, this demonstrated that the method was repeatable. The results are tabulated in Table 3.

Table 3: Precision Data

Sumatriptan Succinate		**Naproxen Sodium**		**Domperidone**	
%Assay		%Assay		%Assay	
99.50 100.64 100.73 101.08 100.61 100.19		99.98 100.77 100.70 99.99 100.79 100.44		100.02 101.83 101.74 101.25 101.06 100.31	
Mean	**100.46**	**Mean**	**100.45**	**Mean**	**101.04**
SD	**0.55**	**SD**	**0.38**	**SD**	**0.738**
%RSD	**0.545**	**%RSD**	**0.375**	**%RSD**	**0.731**

Robustness

The results were not affected significantly and found to be within the acceptance criteria hence the developed method was found to be robust.

CONCLUSION

A new RP-HPLC method for the simultaneous estimation of Sumatriptan Succinate, Naproxen Sodium and Domperidone was developed. The results obtained in the development and validation studies showed that the proposed method is simple, rapid, specific, accurate, precise and robust. It is therefore suitable for the routine analysis of Sumatriptan Succinate, Naproxen Sodium and Domperidone in bulk as well as in pharmaceutical dosage forms. The method can be applied for the analysis of any of the three drugs individually or in two drug combination with one and other.

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