Method Development and Validation for Simultaneous Estimation of Rizatriptan Benzoate and Naproxen Sodium by UV Spectrophotometric Method

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Abstract

A Simple, validated, accurate and precise simultaneous UV Spectrophotometric method has been developed for the simultaneous estimation of Rizatriptan Benzoate (RIZ) and Naproxen Sodium (NAP) in pharmaceutical dosage form. Rizatriptan Benzoate exhibits absorption maximum at 282.9nm and Naproxen Sodium shows absorption maximum at 261.8nm in methanol. The Beer's law obeyed the concentration range of 5-30µg/ml for RIZ and NAP. Mean recovery of 100.25% for RIZ and 99.2%5 for NAP respectively signifies the accuracy of the method. This method can be used for the routine simultaneous estimation of RIZ and NAP in pharmaceutical dosage forms.

Keywords: Rizatriptan benzoate, Naproxen sodium, Estimation, Spectrophotometry, Dosage form

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Introduction

Rizatriptan Benzoate (Fig. 1) is an anti-migraine drug used to treat migraine and is chemically N, N-dimethyl-2- [5-(1*H*-1,2,4-triazol-1-yl methyl)-1*H*-indol-3-yl] ethyl amine benzoate[1]. It is a potent, selective 5-hydroxytryptamine$_{1B/1D}$ (5-HT$_{1B/1D}$) receptor (serotonergic) agonist and induces vasoconstriction possibly by inhibiting the release of calcitonin gene related peptide from sensory neurons in the trigeminal nerve. RIZ is a white crystalline solid, soluble in water. It has a molecular weight of 391.5[2].

Naproxen Sodium (Fig. 2) is aryl acetic acid a member of the group of non-steroidal anti-inflammatory drug with analgesic and antipyretic properties[3] which acts by inhibition of the enzyme complex prostaglandin synthetase with consequent reduction in the synthesis of prostaglandins from arachidonic acid. It is chemically (S)-6-methoxy-α-methyl-2-naphthaleneacetic acid sodium salt[4]. NAP is a White crystalline substance, freely soluble in water at neutral pH. It has a molecular weight of 230.3. Naproxen is commonly used for reduction of pain, fever, inflammation and stiffness caused by conditions including migraine, rheumatoid arthritis, gout, menstrual cramps, tendinitis and bursitis[5]. The role of combining agents for acute migraine treatment has gained attention and the combination of a Rizatriptan and Naproxen has demonstrated better efficacy[6].

A survey of literature reveals that very few simultaneous analytical methods were available for determination of Rizatriptan Benzoate and Naproxen Sodium by using spectrophotometric[7] and liquid chromatographic methods[8]. Hence the objective of the present work is to develop and validate a new, simple, sensitive, specific, precise and accurate UV Spectrophotometric method for the simultaneous determination Rizatriptan Benzoate and Naproxen Sodium in bulk drug and in pharmaceutical formulations.

Materials and Methods

Chemicals and Reagents: The reference samples of Rizatriptan Benzoate (API) and Naproxen Sodium (API) were provided as gift samples from Sumages Pharma Pvt. Ltd., Bhimavaram, India. The commercial formulations (tablets) were not available in local market. Tablets containing 5 mg of Rizatriptan Benzoate and 25 mg of Naproxen Sodium were prepared in-house. Methanol (AR grade) was purchased from E. Merck (India) Ltd., Mumbai, India and was used as solvent. Fresh purified distilled water was used throughout the experiment.

Instruments: Shimadzu UV1800 Double Beam UV-Visible Spectrophotometer was used for spectral studies. Shimadzu BL220H Digital Weighing Balance was used for weighing the materials.

Preparation of standard stock solution: The standard stock solutions of RIZ and NAP were prepared by dissolving accurately weighed 100mg of drug in 100ml of methanol in two separate 100ml volumetric flasks to get concentration of 1mg/ml. A dilution of stock solution was made with methanol to get working standard solution of 100µg/ml of both drugs.

Determination of λ max: The standard solutions of both Rizatriptan and Naproxen (10µg/ml) were scanned in the wavelength region of 200-400nm and the λ max was found to be 282.9nm and 261.8nm for Rizatriptan and Naproxen respectively.

Preparation of calibration curve: Working standard solutions were prepared for the Rizatriptan Benzoate and Naproxen Sodium from the standard solution of 100µg/ml. Different aliquots were taken from standard stock solution and diluted with methanol separately to prepare 5µg/ml, 10 µg/ml, 15 µg/ml, 20 µg/ml, 25 µg/ml and 30 µg/ml solutions respectively. Prepared working solutions of Rizatriptan and Naproxen were scanned at 282.9nm and 261.8nm respectively. The respective absorbance's were recorded and absorbances were plotted against the concentrations to obtain the respective calibration curve.

Assay of tablet dosage form: Twenty tablets were weighed and finely powdered. An accurately weighed portion of powder sample equivalent to 5mg of Rizatriptan Benzoate and 25mg of Naproxen Sodium was transferred into a 100ml clean dry volumetric flask containing 70ml of methanol. The solution was sonicated for 5min and the drug was dissolved completely. The volume was made up to the mark with a further quantity of the methanol to get a stock concentration of Rizatriptan Benzoate and Naproxen Sodium. Further pipette 2ml of the above stock solution into a 10ml volumetric flask and the volume was made up to the mark with the methanol.

Results

The present study was aimed at developing a simple, sensitive, precise and accurate UV spectrophotometric method for the simultaneous estimation of Rizatriptan Benzoate and Naproxen Sodium from bulk samples and their tablet dosage forms. The wavelengths selected in methanol for estimation of Rizatriptan Benzoate were found to be 282.9nm and for Naproxen Sodium was found to be 261.8nm. The linearity was found satisfactory in the concentration range of 5-30µg/ml for Rizatriptan Benzoate (Fig. 3) and 5-30µg/ml for Naproxen Sodium (Fig. 4). The regression equation of the linearity curve between concentrations of Rizatriptan and Naproxen over its absorbance's were found to be y=0.0219x+0.0119 (Table 1) and y=0.0217x+0.0244 (Table 2) respectively with a correlation coefficient (r^2) of 0.9966 for Rizatriptan and 0.9942 for Naproxen. Precision of the method was studied by repeated measurements of drug solution and results showed lower % RSD values. The % RSD for intra-day precision (Table 3) and inter-day precision (Table 4) for Rizatriptan were found to be 0.89% and 0.72% respectively. The % RSD for intra-day precision (Table 5) and inter-day precision (Table 6) for Naproxen were found to be 0.85% and 0.75% respectively.

This reveals that the method is quite precise. The percent recoveries of the drug solutions of Rizatriptan and Naproxen were studied at three different concentration levels. The mean recovery of the drugs Rizatriptan and Naproxen was 100.40% (Table 7) and 99.25% (Table 8) respectively. The limit of detection (LOD) and limit of quantification (LOQ) for Rizatriptan Benzoate were found to be 1.21µg/ml and 3.66µg/ml respectively (Table 9). The limit of detection (LOD) and limit of quantification (LOQ) for Naproxen Sodium were found to be 1.24µg/ml and 3.77µg/ml respectively (Table 10). The percentage purity for the assay of Rizatriptan and Naproxen were found to be 98.48% and 99.72% respectively (Table 11). The assay results showed that the drug contents of this product to be in accordance with the labeled claims. No interfering peaks were found in the absorption spectrum of the tablet formulation indicating that excipients used in tablet formulations did not interfere with the simultaneous estimation of the drugs Rizatriptan and Naproxen by the proposed UV spectrophotometric method.

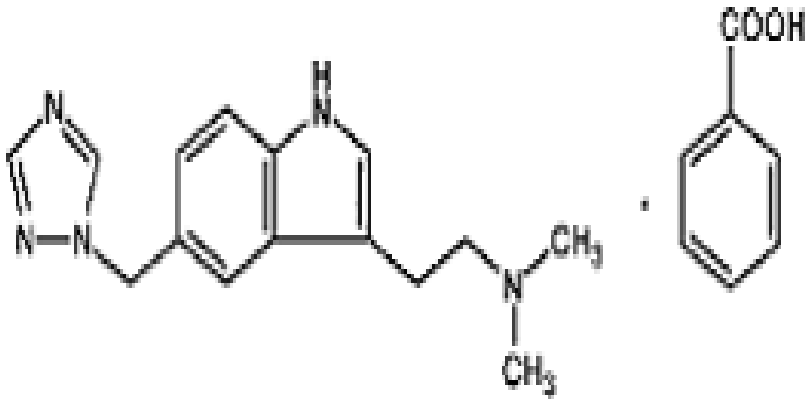

Fig. 1: Molecular structure of Rizatriptan Benzoate

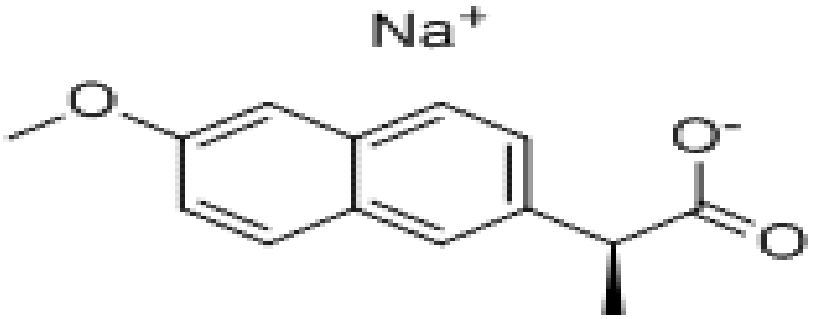

Fig. 2: Molecular structure of Naproxen Sodium

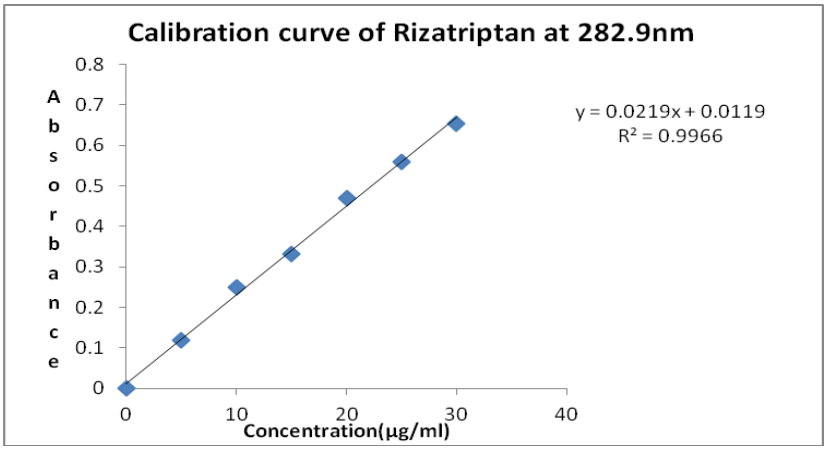

Fig. 3: Calibration curve of Rizatriptan Benzoate

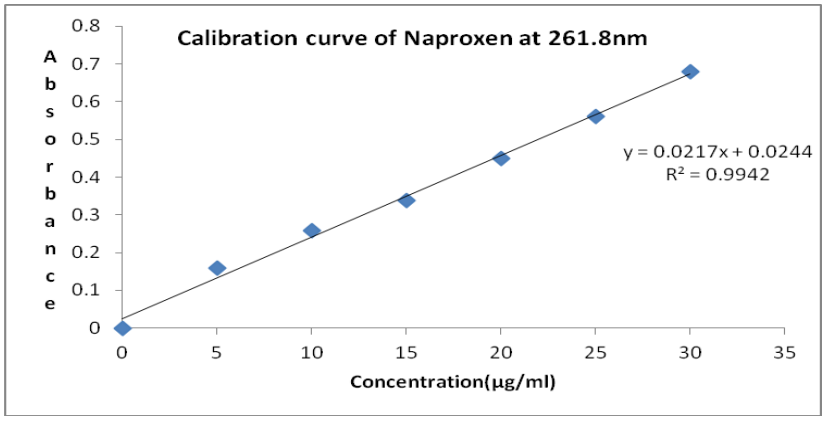

Fig. 4: Calibration curve of Naproxen Sodium

Table 1: Linearity results of Rizatriptan Benzoate

S. No.	Concentration (µg/ml)	Absorbance
1.	0	0
2.	5	0.118
3.	10	0.249
4.	15	0.333
5.	20	0.470
6.	25	0.559
7.	30	0.635
Slope		0.0219
Intercept		0.0119
Regression Equation(y)		0.0219x+0.0119
Correlation Coefficient		0.9966

Table 2: Linearity results of Naproxen Sodium

S. No.	Concentration (µg/ml)	Absorbance
1.	0	0
2.	5	0.160
3.	10	0.258
4.	15	0.337
5.	20	0.450
6.	25	0.559
7.	30	0.680
Slope		0.0217
Intercept		0.0244
Regression Equation(y)		0.0217x+0.0244
Correlation Coefficient		0.9942

Table 3: Intra-day precision results of Rizatriptan Benzoate

S. No.	Time (Hours)	Absorbance
1	0	0.476
2	1	0.492
3	2	0.456
4	3	0.482
5	4	0.462
6	5	0.476
7	6	0.456
	Mean	0.471
	SD	0.008
	% RSD	0.89

Table 4: Intra-day precision results of Naproxen sodium

S. No.	Time (Hours)	Absorbance
1	0	0.462
2	1	0.434
3	2	0.450
4	3	0.438
5	4	0.469
6	5	0.452
7	6	0.449
	Mean	0.450
	SD	0.008
	% RSD	0.85

Table 5: Inter-day precision results of Rizatriptan Benzoate

S. No.	Time (Days)	Absorbance
1	1	0.471
2	2	0.476
3	3	0.469
4	4	0.479
5	5	0.452
6	6	0.472
	Mean	0.469
	SD	0.0034
	% RSD	0.72

Table 6: Inter-day precision results of Naproxen Sodium

S. No.	Time (Days)	Absorbance
1	1	0.451
2	2	0.479
3	3	0.432
4	4	0.452
5	5	0.452
6	6	0.459
	Mean	0.449
	SD	0.0003
	% RSD	0.75

Table 7: Recovery studies for Rizatriptan Benzoate

Level	Standard conc. (µg/ml)	Conc. added (µg/ml)	Conc. found (µg/ml)	% Recovery	% Mean recovery
50%	10	5	5.03	100.66	100.40
100%	10	10	10.1	101.00	
150%	10	15	14.93	99.55	

Table 8: Recovery studies for Naproxen Sodium

Level	Standard conc. (µg/ml)	Conc. added (µg/ml)	Conc. found (µg/ml)	% Recovery	% Mean recovery
50%	10	5	4.95	99.00	99.25
100%	10	10	9.83	98.33	
150%	10	15	15.06	100.44	

Table 9: LOD and LOQ of Rizatriptan Benzoate

Parameter	Measured value (µg/mL)
Limit of detection	1.21
Limit of quantification	3.66

Table 10: LOD and LOQ of Naproxen Sodium

Parameter	Measured value (µg/mL)
Limit of detection	1.24
Limit of quantification	3.77

Table 11: Assay results of Rizatriptan Benzoate and Naproxen Sodium formulations

Formulation	Label claim	Amount found	% Assay
Rizatriptan Benzoate	5mg	4.924mg	98.48%
Naproxen Sodium	5mg	4.986mg	99.72%

Conclusion

In the present investigation, an attempt has been made to develop simple, sensitive, precise and accurate UV spectrophotometric method for the simultaneous determination of Rizatriptan Benzoate and Naproxen Sodium in bulk sample and pharmaceutical formulations. The satisfying recoveries, low correlation coefficient and assay results confirmed the suitability of proposed method for the routine quality control analysis for simultaneous determination of Rizatriptan Benzoate and Naproxen Sodium in pharmaceutical formulations. The method was validated as per International Conference on Harmonization Guidelines and the results are within the limits. To conclude, the UV spectrophotometric method is more economical for analysis of bulk drugs and pharmaceutical formulations.

Source of Support: None

Conflict of Interest: Nil

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