Chemistry Research Journal, 2024, 9(3):9-15
Available online www.chemrj.org

Research Article

ISSN: 2455-8990
CODEN(USA): CRJHA5

Development and Validation of UV Method for the Estimation of Diroximel fumarate in Bulk and Tablet Dosage Form

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Abstract

Diroximel fumarate, sold under the brand name Vumerity, is a medication used for the treatment of relapsing forms of multiple sclerosis (MS). It acts as an immunosuppressant and anti-inflammatory drug. Diroximel fumarate is hypothesized to regulate cell signalling pathways, causing beneficial immune and neuroprotective effects. It is prescribed for the treatment of relapsing forms of multiple sclerosis to include clinically isolated syndrome, relapsing-remitting disease and active secondary progressive disease in adults. The maximum absorbance of drug was found at 210 nm. Diroximel fumarate was found to be dissolved in methanol and distilled water so a ratio of 1:9 was used as solvent for the conduction of work. Linearity range for the method was finalized as 2-10 µg/ml with R2 value of 0.999. % RSD less than 2, which are well within indicates the method is precise and robust. The % recovery rate was found to be 99-101% indicating the method's accuracy. The method was validated as per ICH guidelines provided and the results were found to be satisfactory. LOD & LOQ values were obtained as 0.120 & 0.364 respectively.

Keywords: Diroximel fumarate, vumerity, multiple sclerosis, immunosuppressant, cell signalling

1. Introduction

Spectroscopy is a branch of science that studies the interaction between EMR and matter. The basic law that relates absorbance and concentration is the Beer-Lambert law [1].

Beer-Lambert's law is an essential relationship in spectroscopy that describes the connection between the concentration of a solution and the amount of light absorbed by that solution. The law states that the absorbance (A) of a sample is directly proportional to the concentration (c) of the absorbing species in the sample and the path length of the light through the sample [2,3].

A neurological disease that can cause severe physical and cognitive symptoms, multiple sclerosis (MS) is a chronic and debilitating condition that may significantly decrease quality of life. It is the primary cause of neurological impairment in young adults that is not brought on by trauma. Neurological symptoms in relapsing-remitting MS patients resolve and recur on a regular basis. Over 80% of individuals afflicted with this illness have relapsing-remitting multiple sclerosis [4,5].

Table 1: Drug profile

Criteria	Features
IUPAC name	4-O-[2-(2,5-dioxopyrrolidin-1-yl) ethyl] 1-O-methyl (E)-but-2-enedioate
Molecular formula	$C_{11}H_{13}NO_6$
Molecular weight	255.22 g/mol
λ_{max}	210 nm
Solubility	Soluble in methanol, slightly soluble in water
Brand name	Vumerity (231mg)

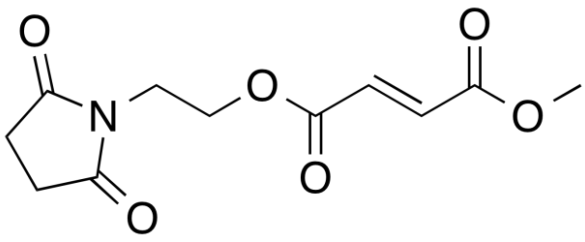

Figure 1: Structure of diroximel fumarate

A search through the literature revealed that the drug has been examined with a variety of analytical approaches, notably RP-HPLC. The development of a basic, precise, reliable, and repetitive UV Spectrophotometric method for the quantification of Diroximel fumarate in bulk and in tablet dosage form is described in the current work. According to ICH Guidelines, the developed approach was validated (6).

Material and Methods

Chemicals and reagents

Pharmaceutical grade API of diroximel fumarate was procured as gift sample. All chemicals and reagents were of analytical grade.

Instrumentation

The proposed work was carried out on TG Ultraviolet visible spectrophotometer, T-60 Model, which is a double beam double detector configuration with a 1 cm quartz matched cell. All weighing was done on PGB-200 model weighing balance.

Selection of solvent [7,8]

On the basis of solubility study methanol: water in the ratio of 1:9 was selected as the solvent for dissolving diroximel fumarate.

Method development [9-12]

Preparation of standard stock solution

Stock solution A (1mg/ml): Accurately weighed 10mg of diroximel fumarate in to a 10ml volumetric flask, dissolved in 1ml methanol and made up the volume to 10ml with water.

Stock solution B (100µg/ml): 5 ml of stock solution A was taken and diluted up to 50 ml with water.

Dilutions: Further serial dilutions were done by taking 0.2, 0.4, 0.6, 0.8, 1 ml of stock B and made up the volume with water up to 10ml to give concentrations 2, 4, 6, 8, 10 µg/ml.

Selection of analytical wavelength

An appropriate aliquot portion of 0.6 ml from stock solution B was transferred to 10 mL volumetric flasks; the volume was made up to the mark using Water (6 µg/ml - working standard). Drug solution was scanned against blank between 200 nm to 400 nm range. The drug showed λ_{max} at 210nm.

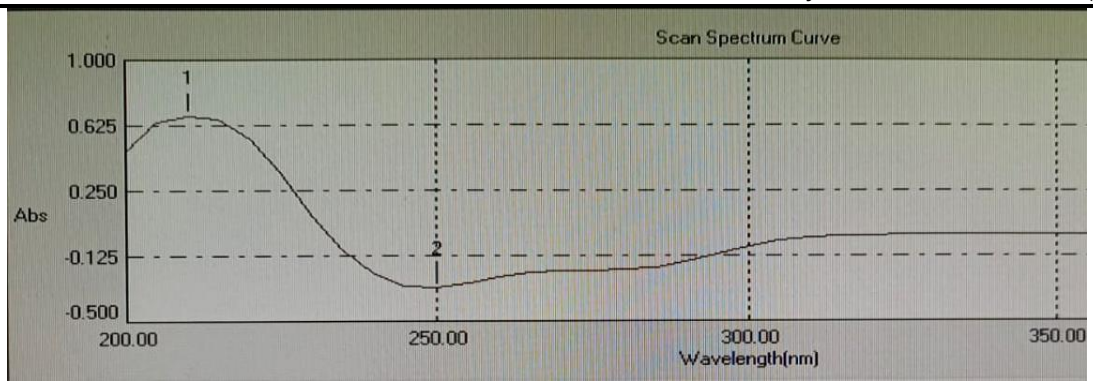

Figure 2: UV spectrum of diroximel fumarate (210 nm)

Method validation

The suggested approach has undergone rigorous validation in terms of linearity, accuracy, precision, limits of detection (LOD) and quantification (LOQ), robustness, ruggedness and assay.

Determination of linearity

A working standard solution of the drug was divided into five separate 10 mL volumetric flasks using an appropriately measured proportionate fraction. Water was used to make up the volume to the required level in order to produce concentrations (2–10 µg/mL). The absorbance of these solutions was measured at 210 nm. The calibration curve was displayed in a concentration versus absorbance graph.

Accuracy

On the basis of a recovery, research carried out using the conventional addition approach, the proposed method's accuracy was determined. The tablet powder was re-analysed using the recommended method after being mixed with a known quantity of standard medication solutions to make final concentrations of 50%, 100%, and 150%. The absorbance recorded and the % recoveries were calculated.

Precision

Precision was determined as intra-day and inter-day variations. The results of the intra-day and inter-day precision research were determined by calculating absorbance at the same drug concentrations (6 ppm) three times on the same day and three different days over the course of a week at a wavelength of 210nm. The results were reported.

Ruggedness

The suggested method's durability was assessed through the analysis of portions from uniform slots by two different analysts under similar operational and environmental circumstances. The results were reported accordingly.

Robustness

Robustness was obtained by performing the analysis at two different wavelengths (±5 nm). The results were reported.

LOD & LOQ

LOD & LOQ gives information about the sensitivity of the method. The values reported indicate that the method is highly sensitive.

Results and Discussion

Assay

Table 2: Assay results

Formulation	Label claim mg/tab	Amount found Mean ± S.D.	Assay	%RSD
Tablet	231	99.89 ± 0.0064	99.89%	0.0064

Method Validation

Linearity

The calibration curve has a regression coefficient of 0.999 and displayed linearity in the 2–10 µg/ml range.

Table 3: Linearity of diroximel fumarate

S. No.	Diroximel Fumarate	
	Concentration	Absorbance
1	2	0.144
2	4	0.251
3	6	0.343
4	8	0.443
5	10	0.546
	y=0.498x+0.0466 (Regression equation)	
R^2	0.999	

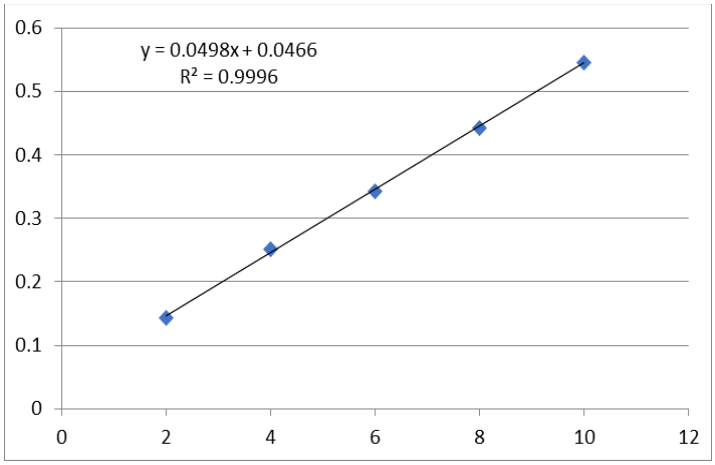

Figure 3: Calibration curve of diroximel fumarate

Accuracy

The % RSD of the present work was found to be within and less than 2. The %Recovery was between 99-101%.

Table 4: Accuracy data

% Sample spiked	Sample (Tablet)	Standard (6 PPM)	Mean	SD	%RSD	%Recovery
50%	1.5	0.75	0.486	0.0011	0.237	99.54
	1.5	0.75				
	1.5	0.75				
100%	1.5	1.5	0.634	0.0005	0.0909	100.22
	1.5	1.5				
	1.5	1.5				

150%	1.5	2.25	0.779	0.0005	0.0740	99.69
	1.5	2.25				
	1.5	2.25				

Precision

The % RSD of Diroximel fumarate was found to be 0.150 for intraday precision and 0.183 for interday precision respectively.

Table 5: Intraday precision

	10AM Mean± SD	**%RSD**	**1PM Mean ±SD**	**%RSD**	**4PM Mean ±SD**	**%RSD**
LQC (2PPM)	0.144333± 0.000516	0.357781	0.144667± 0.000516	0.356957	0.1445± 0.000548	0.379047
MQC (6PPM)	0.000548± 0.159453	0.159453	0.344± 0.000632	0.183853	0.343667± 0.000516	0.150261
HQC (10PPM)	0.000548± 0.100407	0.100407	0.544667± 0.000816	0.149908	0.545167± 0.000753	0.138081

Table 6: Interday precision

	10AM Mean± SD	**%RSD**	**1PM Mean ±SD**	**%RSD**	**4PM Mean ±SD**	**%RSD**
LQC (2PPM)	0.1445± 0.000837	0.579003	0.145± 0.000632	0.436176	0.145± 0.144833	0.519751
MQC (6PPM)	0.343667± 0.000816	0.237584	0.344167± 0.000753	0.218723	0.344± 0.000632	0.183853
HQC (10PPM)	0.544833± 0.001169	0.214569	0.545± 0.000894	0.164115	0.545167± 0.000983	0.180347

Robustness

A small variation of the wavelength (±2nm) was applied to the presented method and it was found that the %RSD was within the limits and the values were 0.168 and 0.291.

Table 7: Robustness

Conc. (µg/ml)		**215nm**	**225nm**
6	Mean	0.342667	0.343
6	SD	0.000577	0.001
6	%RSD	0.168487	0.291545

Ruggedness

Two different analysts performed the ruggedness studies under same conditions and it was found that the % RSD was within the limits.

Table 8: Ruggedness

Conc. (µg/ml)		**Analyst-1**	**Analyst-2**
6	**Mean**	0.344333	0.343333
6	**SD**	0.000577	0.001155
6	**%RSD**	0.167672	0.336321

LOD & LOQ

The study for LOD & LOQ was carried out and the obtained results are described in the table below:

Table 9: LOD & LOQ

Drug	LOQ	LOD
Diroximel Fumarate	0.1204 µg/ml	0.3649 µg/ml

Using UV Spectrophotometry, we created a method in this work for estimating diroximel fumarate in both bulk and pharmaceutical dosage forms. With the use of various techniques like HPLC there have been numerous methods. We used UV Spectrophotometry to carry out the method's development and validation which is fast and economical.

Conclusion

Based on the afore mentioned findings, it can be said that the suggested method is straightforward, sensitive, exact, repeatable, and affordable to determine Diroximel fumarate in bulk and tablet dosage form. The drug R^2 value is 0.999 indicates the method is linear, and a %RSD of less than 2 suggests the method is robust and precise. The lowest LOD value determines the method's sensitivity. The developed method is developed and validated as per ICH guidelines and it can be used for routine analysis of diroximel fumarate.

Competing interest statement

All authors declare that there is no conflict of interests regarding publication of this paper.

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