



DEVELOPMENT AND VALIDATION OF UV SPECTROPHOTOMETRIC AREA CURVE METHOD FOR QUANTITATIVE ESTIMATION OF SONIDEGIB IN BULK AND CAPSULE DOSAGE FORM

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ABSTRACT

A simple UV method was developed for the determination of sonidegib in bulk and capsule dosage form. The aim of this work is to develop a simple, accurate, reproducible and cost effective. This method is based on area under curve (AUC) in wavelength range between 272 – 282nm and method has linearity in the concentration range of 10 – 50 µg/ml. Methanol was used as solvent. The developed analytical method was validated as per International Conference on Harmonization (ICH) guidelines. The value of correlation coefficient (R^2) was 0.9999. Results of the recovery studies showed good accuracy of the method.

KEYWORDS: Sonidegib, UV Spectrophotometry, Area under curve (AUC), Validation.

INTRODUCTION

Sonidegib (Figure 1), chemically N-[6-(cis-2,6-dimethylmorpholin-4-yl)pyridin-3-yl]-2-methyl-4-(trifluoromethoxy) [1,1'-biphenyl]-3-carboxamide.^[1] It inhibit activation of the Hedgehog pathway. Sonidegib is primarily metabolized by CYP3A and is eliminated hepatically.^[2]

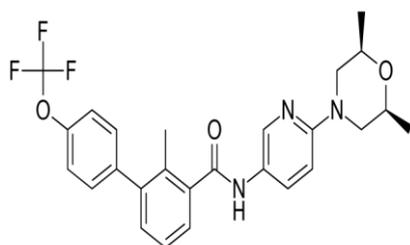


Fig. 1: Chemical structure of Sonidegib.^[3]

On literature survey, No method was reported for the estimation of Sonidegib by Area under curve method. So we have developed a novel, simple, rapid, accurate, precise, economical and highly sensitive Area under curve method by UV spectroscopy for assay of Sonidegib in bulk and capsule dosage form according to ICH guidelines.^[4,5]

MATERIALS AND METHODS

Instrumentation

The instrument used in the present study was Shimadzu double beam UV/Visible spectrophotometer (Model UV-1700) with spectral band width of 1 nm. All weighing was done on electronic balance (Model Shimadzu AUX - 220).

Reagents and Chemicals

Analytically pure sample of Sonidegib was supplied by Beijing mesochem technology co. ltd. (China). The pharmaceutical dosage form used in this study was Odomzo capsule contains equivalent to 200 mg of Sonidegib per capsule. The solvent used was methanol.

Selection of wavelengths for estimation

In UV spectrophotometric method, solution of Sonidegib (10 µg/ml), was prepared by appropriate dilution of standard stock solution with methanol and scanned in the spectrum mode from 200 nm to 400 nm. From the absorption spectrum, the wavelength selected for area under curve of wavelength ranging between 272 – 282 nm.

Preparation of standard stock solution

200mg of Sonidegib was weighed accurately and it transferred in to 100ml volumetric flask then volume was

made with methanol up to the mark, the obtaining concentration was 2000 μ g/ml.

Preparation of working standard solution

From above standard stock solution of Sonidegib, 1ml of solution was taken into 100 ml volumetric flask and was made to the mark with the mobile phase to get 20 μ g/ml of Sonidegib.

METHOD

AREA UNDER CURVE (AREA CALCULATION):

In this method area calculation involves calculation of integrated value of absorbance with respect to wavelengths. Area calculation processing item calculates the area bounded by the curve and horizontal axis. In this study area was integrated between wavelengths ranges from 272 to 282nm. The spectra of Sonidegib is shown in Fig.No.2.

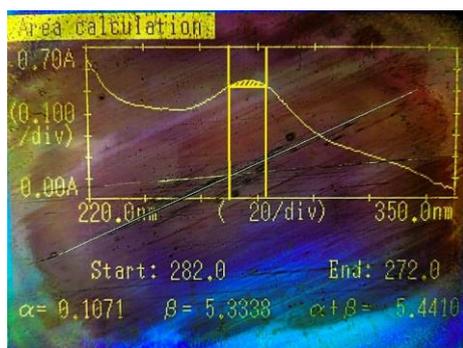


Fig. 2: The Wavelength ranges from 272 – 282 nm in UV Spectru.

Analysis of Marketed Capsule Formulation

For the estimation of drug in commercial formulation, twenty capsules were weighed and average weight was calculated. Each capsule dosage form containing 200 mg of Sonidegib. An accurately weighed portion of powder sample equivalent to 200mg was transferred into a 100 ml clean dry volumetric flask containing 70 ml of methanol. The contents of the flask were sonicated for 10 min and the volume was made up to the mark with a further quantity of the methanol to get a stock concentration of Sonidegib (2000 μ g/ml). Further pipette 1.0 ml of the above stock solution into a 100 ml volumetric flask and the volume was made up to the mark with the methanol to get concentration of 20 μ g/ml. The concentration of Sonidegib was determined by measuring the area under curve of the sample solution in wavelength ranging between 272 – 282 nm. Concentration of Sonidegib in the diluted solution was obtained from calibration curve. Amount of Sonidegib in

mg/cap was then calculated, by multiplying the concentration obtained with dilution factor.

Validation

The proposed methods were validated as per ICH guidelines.

Linearity

Different aliquots of 0.5-2.5 ml of Sonidegib was transferred into series of 100 ml volumetric flasks, separately and the volume was made up to the mark with Methanol to get concentrations 10, 20, 30, 40 and 50 μ g/ml, respectively. In this study area was integrated between wavelength ranges from 272 – 282nm.

Precision

Precision was evaluated at the repeatability and intermediate precision levels. For repeatability analysis, six independent portions of a capsule dosage form were processed through the full analytical method and results was evaluated obtaining a % RSD value of 0.0054 as shown in table 2.

Accuracy

Accuracy of the proposed method was determined by performing the recovery experiment. The recovery experiment was studied by adding known amount of standard sonidegib to the pharmaceutical product and calculating the recovered standard amount. At 50%, 100% and 150% standard addition level mean recovery of sonidegib found to be 99.66%, 100.05% and 99.50% respectively. The results of recovery experiment are given in table 3.

RESULTS AND DISCUSSION

The methods discussed in the present work provide a convenient and reliable way for quantitative determination of Sonidegib in capsule formulation. The wavelength range selected was 272 - 282 nm. The optical characteristics of sonidegib was shown in table 1. Percent label claim for Sonidegib in capsule analysis was found to be 99.96% as shown in Table 2. Percent recovery for Sonidegib, was found to be 99.66% to 100.05% indicating accuracy of this methods as shown in Table 3. Intra-day and Inter-day precision studies were carried out by analyzing capsule formulation, three times on the same day and on three different days, respectively. Standard deviation and coefficient of variance for intra-day and inter-day precision studies was satisfactorily low indicating high degree of precision and reproducibility of this methods.

Table 1: Optical Characteristics Of Sonidegib (Area Under Curve Method).

PARAMETERS	AT 272 nm – 282 nm*
Beer's law range (μ g/ml)	10-50
Regression equation ($y = mx + c$)	$y = 0.5057x + 0.0012$
Loss of detection (μ g/ml)	0.0018
Loss of quantification (μ g/ml)	0.0055
Sandells sensitivity (μ g/cm ² /0.001 A.U)	0.0019

Standard error	0.0081
Correlation coefficient (r)	0.9999

Table 2: Results of analysis of capsules.

Sample	Sample number	Label claim (mg/cap)	Amount present (mg/cap)*	% Purity* (% w/w)	Mean purity (% w/w)	SD	% RSD
SONIDEGIB	1	200	200.03	100.32	99.96	0.5494	0.0054
	2	200	200.05	100.16			
	3	200	200.00	99.52			
	4	200	200.01	100.74			
	5	200	200.00	99.24			
	6	200	200.03	99.82			

Table 3: Results of recovery studies for formulation.

S.NO	Percentage of sample taken (%)	Amount of sample added (µg/ml)	Amount of standard added (µg/ml)	Amount recovered (µg/ml)	%Recovery	%RSD
1	50	20	10	29.89	99.66	0.7299
2	100	20	20	40.02	100.05	0.3463
3	150	20	30	49.75	99.50	0.3009

CONCLUSION

The proposed UV spectrophotometric method by Area under curve was employed here proved to be simple, economical, rapid, precise and accurate. Thus these can be used for routine estimation of Sonidegib in capsule dosage form.

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