

Research Article

Formulation and Evaluation of Chewable Tablets of Catharanthus Roseus Leaf

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Resmetirom is a selective thyroid hormone receptor- β agonist which has been recently approved for the treatment of metabolic associated steatohepatitis (MASH). This article was aimed at developing and validating a simple, accurate, precise and economical zero-order and first-order derivative UV spectrophotometric method for estimation and validation of Resmetirom in bulk and tablet dosage form. Methanol and distilled water are selected as solvents which are used in 1:9 ratio. Resmetirom showed maximum absorbance at 300 nm in zero-order and 217nm in first-order derivative spectra. Linearity was checked using 2-12 μ g/ml as concentration range and was found to be linear. Validation was carried out according to ICH Q2 (R1) guidelines. The developed methods showed good accuracy, precision and sensitivity with % RSD values less than 2. The developed methods are simple, cost effective and suitable for routine quality control analysis in Resmetirom.

Keywords: Resmetirom, Methanol, UV spectrophotometry, Derivative spectroscopy, Method validation, ICH guidelines.

INTRODUCTION

Metabolic associated steatohepatitis (MASH), previously known as Non-alcoholic associated steatohepatitis (NASH) is a non-alcoholic liver disease which involves moderate to advance liver fibrosis. Resmetirom is a selective thyroid hormone receptor (THR- β) agonist, a first approved drug for the treatment and management of MASH (Metabolic

Associated Steatohepatitis) [1]. Resmetirom is a recently FDA approved drug which is chemically represented as 2-(3,5-dichloro-4-{{[6-oxo-5-(propan-2-yl)-1,6-dihydropyridazin-3-yl]oxy}phenyl}-3,5-dioxo-2,3,4,5-tetrahydro-1,2,4-triazine-6-carbonitrile. Molecular weight of Resmetirom is 435.22 and has molecular formula of C₁₇H₁₂Cl₂N₆O₄ [6].

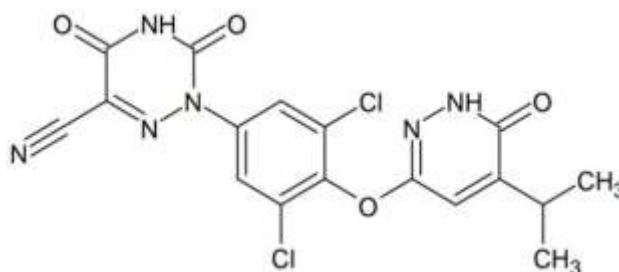


Figure 01: Structure of Resmetirom

Resmetirom act on THR- β present in the liver and activates it. Activation of this receptor leads to

increased hepatic fat metabolism, enhances mitochondrial β -oxidation and reduces lipotoxicity.

Due to these functions, it leads to decrease in hepatic fat content, inflammation and fibrosis progression associated with NASH (Non-alcoholic steatohepatitis) which is now termed as MASH (Metabolic associated steatohepatitis) [4]. It is used for treating moderate to advanced liver fibrosis in adults and is recommended along with proper diet and exercise [5]. According to literature survey, there are very limited methods developed under UV spectroscopy. The aim of this research is to develop a UV spectrophotometric method which is a simple, accurate and precise method for validating a drug. Both zero order and first order derivative spectrophotometric methods have been developed and validated according to ICH guidelines [2, 3].

MATERIALS AND METHODS:

Chemicals and reagents:

Standard Resmetirom API and formulation are obtained as Gift sample from Micro Labs, Bangalore. Solvents such as Methanol and distilled water of analytical grade were used throughout the study. Methanol and distilled water in the ratio of 1:9 act as a solvent system.

Instruments:

Shimadzu AUX-200 analytical balance was used for weighing. Ultrasonication was carried out using laboratory sonicator model 2120. UV analysis was performed using Shimadzu UV-1700 double beam UV-Visible spectrophotometer with a pair of 10mm matched quartz cells and wavelength range lies between 200-400nm.

Selection of solvent:

Solubility studies showed that Resmetirom was freely soluble in Methanol and slightly soluble in distilled water. As methanol is of high cost, for economic purpose we used ratio solvent system. A mixture of Methanol and distilled water in the ratio of 1:9 is selected as a suitable solvent system.

Preparation of standard stock solution:

An accurately weighed 10mg of Resmetirom was transferred into 100ml volumetric flask and dissolved

with 10ml of methanol and the volume was made up with distilled water to obtain a concentration of 100µg/ml. Working standard solution was prepared by further dilution of standard stock solution to get final volume of 20µg/ml.

Selection of wavelength:

The standard stock solution was diluted with distilled water to get final concentration of 10 µg/ml of Resmetirom and was scanned between 200-400nm of standard UV-Visible spectrophotometric range. The maximum absorbance of solution was observed at 300nm in Zero order spectrum. This spectrum was derivatized to first order spectrum in which the maximum absorbance was observed at 217nm.

Preparation of Calibration curve:

From the working standard solution of Resmetirom (20 µg/ml) pipetted out 1 ml, 2 ml, 3 ml, 4 ml, 5 ml, 6 ml and was transferred into series of six 10 ml volumetric flasks and dilute with distilled water to obtain a concentration in the range of 2-12 µg/ml. The absorbance of these concentrations were measured at 300 nm for Zero order, which is derivatized to first order, and measured at 217 nm. The calibration curve was plotted between concentration and absorbance.

Analysis of Marketed Tablet Formulation:

Weigh 20 tablets of Resmetirom with label claim of 60mg and powdered. Tablet powder equivalent to 10mg of Resmetirom was transferred into 100ml volumetric flask and dissolved using methanol with an aid of sonication for around 15 minutes and filtered with the aid of Whatmann filter paper. The solution is then diluted with distilled water. The solution was further diluted with distilled water to get final concentration 6 µg/ml of Resmetirom. The absorbance of the solution was measured at 300 nm for zero order that is derivatized to first order and the absorbance was measured at 217 nm. The procedure was repeated for 6 times.

Recovery studies:

The recovery studies were done by adding known concentration of Resmetirom raw material to pre-analysed formulation. The tablet powder equivalent to

10 mg of Resmetirom was weighed accurately, transferred into a series of three 100 ml volumetric flask, and dissolved with methanol and then ultrasonication was performed for 20 mins and made up the volume with distilled water to get 100µg/ml. The solution was filtered through Whatmann filter paper No. 41 and further diluted with distilled water to get 6µg/ml. To that solution, raw material of Resmetirom were added at 80 %, 100 % and 120 % levels and dissolved with minimum quantity of distilled water and made with the same solvent. Absorbance was measured at 300 nm for zero order and it is derivatized to first order and measured at 217 nm. The amount of drug recovered from the formulation was calculated for all concentrations.

Method validation:

The developed methods Zero order and derivatized first order were validated as per ICH Q2 (R1) guidelines for linearity, accuracy, precision (interday and intraday), Limit of Detection (LOD), Limit of Quantification (LOQ) and ruggedness of Resmetirom are studied according to guidelines and ensured that the limits are within the specified range.

Linearity:

Concentration range of 2-12µg/ml was selected was evaluating the linearity of Resmetirom. The calibration curve plotted between concentration and absorbance showed good linearity for both zero order and derivatized first order with squared correlation coefficient (R^2) greater than 0.999, which complies with the Beer's law. The linearity was calculated by the least square regression method and calculated optical parameters of Resmetirom like slope, intercept and correlation coefficient are obtained from zero and first order calibration curves.

Precision:

The reproducibility of the method was confirmed by analyzing the tablet (Intra-day precision) at different time intervals on same day in six times and (Inter-day precision) on six different days. The % RSD values of both zero and first order was found to be less than 2% indicating good precision of the method.

Ruggedness:

Ruggedness of the method was confirmed by analysis of formulation by different analyst and carried out in different instruments. The amount of drug and the percentage RSD values for zero order and derivatized first order.

Accuracy:

Accuracy of the developed method was determined by calculating % recovery at three different levels of 80%, 100% and 120% in pre-analysed samples by using standard addition technique. The results of recovery studies were shown in table 04 for zero and derivatized first order.

RESULTS AND DISCUSSION:

Resmetirom was validated by using zero order and derivatized first order UV spectrophotometric method. The results obtained from the detailed study of drug on reference with ICH recommendations are satisfactory. Methanol and distilled water was selected as a solvent for the estimation of RES-1. The stability study of Resmetirom was carried out in chosen solvent mixture methanol: distilled water (1:9), which was stable upto 3 hours. The standard solution of Resmetirom 10 µg/ml was scanned in UV region between 200 – 400nm. The maximum absorbance of solution was observed at 300nm in Zero order spectrum shown in figure-02. This spectrum was derivatized to first order spectrum in which the maximum absorbance was observed at 217nm shown in figure-03. The different aliquots of RES-1 were prepared in the concentration range from 2-12 µg/ml, the absorbance of solution was observed at 300nm for zero order and derivatized to first order spectrum then observed the absorbance of the solution at 217 nm. The linearity procedure was repeated for six times. From the linearity analysis, the calibration curve was plotted by using concentration and absorbance and shown in Fig-04 for zero order and Fig-05 for derivatized first order. The optical characteristics like correlation coefficient, slope, intercept, LOQ, LOD, molar absorptivity and sandell's sensitivity were calculated, and shown in Table-01 for zero order and derivatized first order. The squared correlation coefficient (R^2) was found to be 0.9998 for zero order and 0.9999 for derivatized first order. This indicates that the drug obey Beer's Law in selected concentration range. The precision of the method was

confirmed by Intraday and Interday analysis. The analysis of the formulation was made 6 time in same day and one time in 6 consecutive days and the percentage RSD values for Intraday and Interday were found to be 0.8862, 1.1256 for zero order (300 nm) and 1.4673, 1.2516 for derivatized first order (217 nm) and shown in Table-02. The developed method was validated for Ruggedness. It refers to the specific of one lab to multiple days, which may include multiple analysts, multiple instruments and different sources of reagents and so on. In the present work, it was confirmed by different analysts and performed in different instruments. The percentage RSD values by analyst 1 and analyst 2 were found to be 0.9285, 0.8691 for zero order and 1.4560, 1.2596 for derivatized first order. The percentage RSD values by Instrument 1 & 2 were found to be 0.9661, 0.8126 for zero order and 1.4671, 1.3700 for derivatized first order and shown in Table-03. This low percentage RSD values indicates that the developed methods has good precision. The Percentage recovery was found to be in range of 99.02-100.25 % for zero order (300 nm) and 99.60-100.95 % for derivatized first order (217 nm). The percentage RSD values of formulation indicate the method is very accurate. The recovery data is shown in Table- 04. The validated UV spectroscopic method employed in this study proved to be simple, economical, rapid, precise and accurate. Therefore, this analytical technique can be effectively applied for the routine estimation of Resmetirom in tablet dosage form.

CONCLUSION:

The analysis of Resmetirom in bulk and tablet dosage form was accomplished through the development and validation of simple, accurate and economical Zero-order and First-order derivative UV Spectrophotometric methods. The methods are validated in accordance with ICH guidelines and satisfactory results were obtained for all validation parameters. Due it's accurate, precise and cost-effectiveness the developed methods can be routinely carried out in laboratories for quality analysis.

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REFERENCES

1. Ali Mohamed Mousa, Mervat Mahmoud, Ghaida Mubarak AlShuraiaan, "Resmetirom: The First Disease-Specific Treatment for MASH", Wiley-International Journal of Endocrinology 2025; 1-7.
2. International Conference Harmonization (ICH) of Technical Requirements for the Registration of Pharmaceuticals for Human use. Validation of Analytical Procedures, ICH-Q2A, Geneva, 1995
3. International Conference on Harmonization (ICH) of Technical Requirements for the Registration of Pharmaceuticals for Human Use. Validation of Analytical Procedures for Human use. Methodology, ICH-Q2B, Geneva, 1996.
4. Muhammad Mazhar Azam, Sameen Mukhtar, Muhammad Haris, Fatima Laique, Suhaina Amir, Mubashir Mohiuddin, Bibek Giri , "FDA's approval of Resmetirom (Rezdiffra): a breakthrough in MASH management Exploration of drug science", Explor Drug Sci. 2024;2:867–874.
5. Resmetirom, ELSEVIER – Clinical Therapeutics 46.2024; 515-516.
6. Sharayu.J. Ghode, Swati, A. Moon, Sahil. S. Ghuge, "A systemic review on Resmetirom for treatment of Non-Alcoholic steatohepatitis", International journal of research publication review .2025; 6(1), 265-271.

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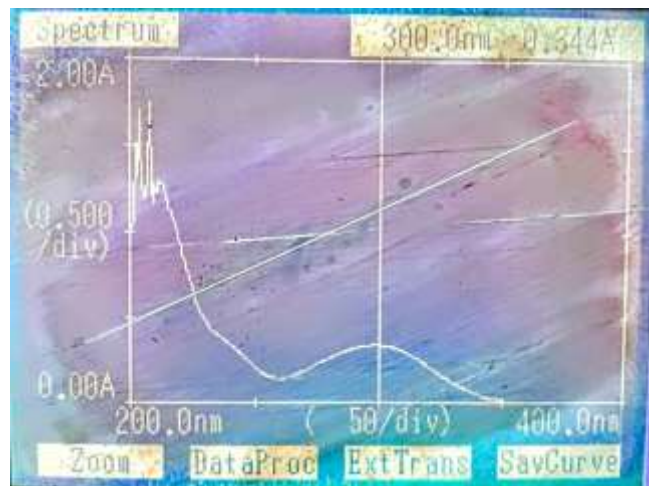


Figure 02: UV spectrum of Resmetirom in methanol: distilled water (1:9) at 300 nm



Figure 03: UV spectrum of Resmetirom in methanol: distilled water (1:9) at 217 nm

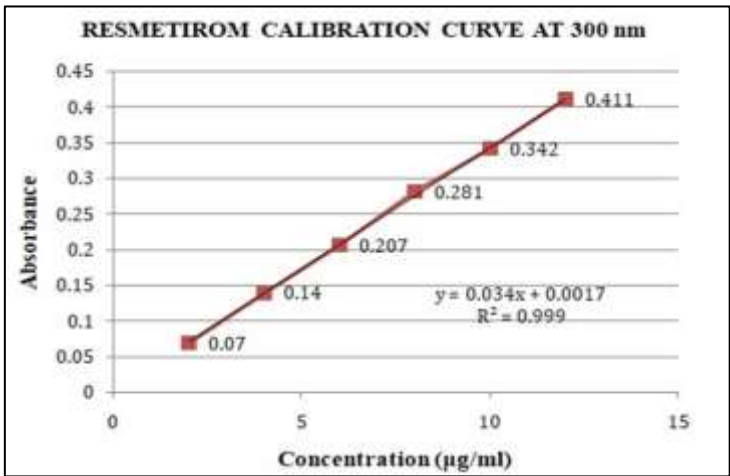


Figure 04: Zero order calibration curve of Resmetirom at 300 nm

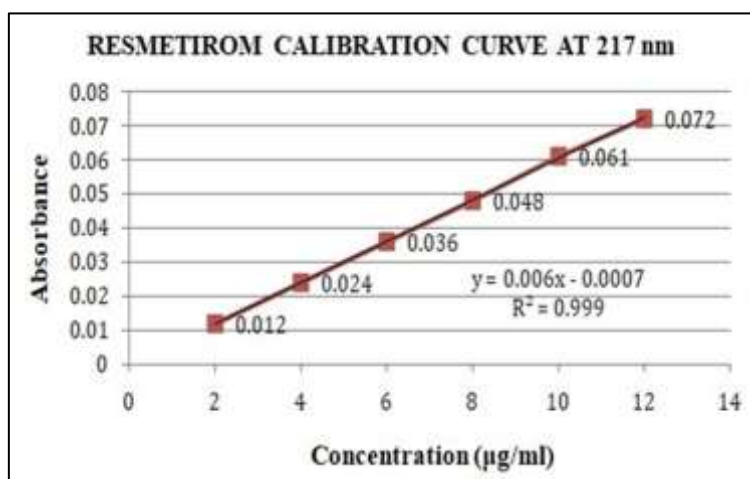


Figure 05: First order calibration curve of Resmetirom at 217 nm

Table 01: Optical characteristics of Resmetirom of Zero order (300 nm) & First order (217 nm)

Parameters	Zero Order	First Order
Beer's law range(µg/ml)	2-12	2-12
Molar absorptivity (L mol ⁻¹ cm ⁻¹)	149344.97	26637.55
Regression Equation (y = mx+c)	y= 0.0342x+0.0017	y=0.0060x-0.000071
Slope(m)	0.0342	0.0060
Intercept(c)	0.0017	-0.000071
Correlation coefficient(r ²)	0.9998	0.9999
Sandell's sensitivity (µg/cm ² /0.001 A.U)	0.0291	0.1656
LOD(µg/ml)	0.2697	0.2073
LOQ(µg/ml)	0.8175	0.6283

Table 02: Precision of Resmetirom of Zero order (300 nm) & First order (217 nm).

Precision parameter	%RSD of Resmetirom	
	Zero order	First order
Repeatability	0.9318	1.4560
Intraday	0.8805	1.4671
Interday	1.1230	1.2514

Table 03: Ruggedness of Resmetirom of Zero order (300 nm) & First order (217 nm)

Type of ruggedness	%RSD	
	Zero order	First order
Analyst-1	0.9285	1.4560
Analyst-2	0.8691	1.2596
Instrument-1	0.9661	1.4671
Instrument-2	0.8126	1.3700

Table 04: Recovery analysis of Resmetirom of Zero order (300 nm) & First order (217 nm)

Concentration	Zero order			First order		
	Average % recovery	SD	%RSD	Average % recovery	SD	%RSD
80%	99.16	0.6250	0.6302	99.60	1.3914	1.3969
100%	100.25	0.8874	0.8851	100.95	1.1200	1.1094
120%	99.02	0.4150	0.4191	100.06	1.3279	1.3271