



“DEVELOPMENT AND VALIDATION OF UV SPECTROPHOTOMETRIC METHODS FOR DETERMINATION OF MEGLUMINE IN BULK”

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ABSTRACT -

UV, first, second and third derivative spectrophotometric methods have been developed for the determination of meglumine. The solutions of standard and sample were prepared in distilled water. For the first method i.e. calibration curve UV spectrophotometric method, the quantitative determination of the drug was carried at 254 nm and the linearity range was found to be 10 – 60 µg/ml. For the first, second, third derivative spectrophotometric methods the drug was determined at 247 nm, 216 nm, 266 nm with the linearity range 10 – 60 µg/ml. The calibration graphs constructed at their wavelength of determination were found to be linear for UV and derivative spectrophotometric methods. All the proposed methods have been extensively validated. There was no significant difference between the performance of the proposed methods regarding the mean values and standard deviations.

Keywords: UV spectrophotometry; Third derivative spectrophotometry; Meglumine.



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1. INTRODUCTION

Chemically Meglumine is 1-Deoxy-1-(methylamino)-D-glucitol. It acts as contrast media and it was also used as veterinary anti-inflammatory drug and used in treatment of leishmaniasis and also used as contrast media ^{1,4}.

The literature survey reveals that Meglumine was analysed by HPLC, NMR spectroscopy was used for determination of Meglumine ^{2,3}. There are no UV and derivative spectrophotometric methods reported for the analysis of meglumine in bulk. Derivative spectrophotometry is an analytical technique of great utility for extracting both qualitative and quantitative information from spectra composed of unresolved bands, and for eliminating the effect of baseline shift and baseline tilts. It consists of calculating and plotting one of the mathematical derivatives of spectral curve. The derivative spectrophotometry is now a reasonable prized standard feature of modern micro – computerized UV spectrophotometry ⁶. The aim of this method was to develop and validate UV calibration curve, first, second and third derivative spectrometric methods for determination of meglumine in bulk.

Analysis is an important component in the formulation development of any drug molecule. It becomes essential to develop a simple, sensitive, accurate, precise, reproducible method for the estimation of drug sample. Our main concern is development and validation of UV, first, second and third derivative spectrometric methods for determination of meglumine in bulk.

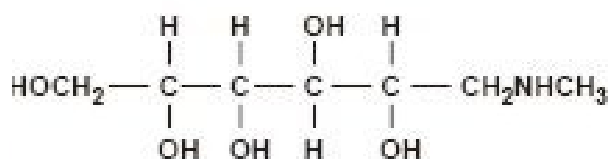


Fig 1: Structure of Meglumine ⁴

2. MATERIAL AND METHODS –

2.1 Instruments and Material -

The instruments used were UV-1800 UV Spectrophotometer SHIMADZU-120 with UV -1800 UV Spectrophotometer ENG 240V Software. Meglumine pure drug and all chemicals and reagents used were of analytical grade.

2.2 Method-

2.2.1. Preparation of Standard Stock Solution

Accurately weighed 100 mg of drug was transferred to 100 ml volumetric flask. It was dissolved in 25 ml of distilled water and finally volume was made up to the mark with same solvent to obtain solution of concentration 1000 µg/ml. Then 1ml solution from this solution was transferred in 10 ml volumetric flask and volume was made up to the mark by distilled water to obtain 100 µg/ml ⁵.

2.2.2. Determination of λ_{max} for Development of Calibration Curve and Derivative Methods

From the stock solution, 1 ml of meglumine was transferred to 10 ml volumetric flask and the volume was adjusted to the mark with distilled water to obtain strength 10 µg/ml. The solution was scanned in the UV range 200-400 nm.

Determination wavelength for first, second and third derivative The normal UV spectra of λ_{max} 254 nm was derivatised into first, second and third order derivative, using UV probe software of instrument. The amplitude of corresponding troughs was measured at 247 nm, 216 nm, 266 nm.

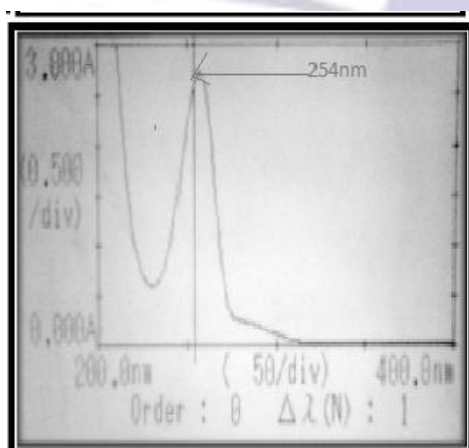


Fig 2: Normal UV spectrum

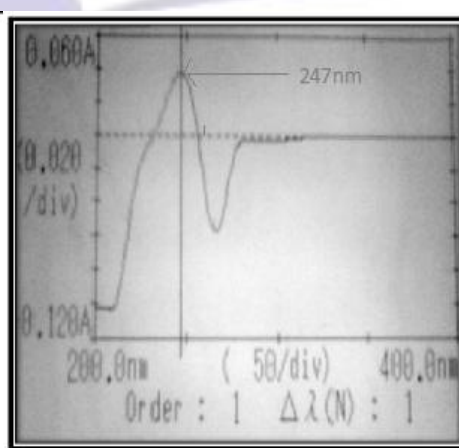


Fig 3: First order derivative spectrum

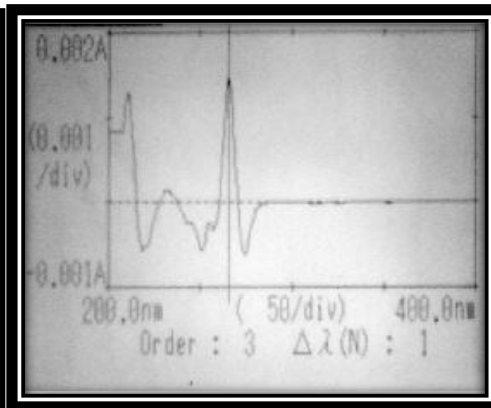
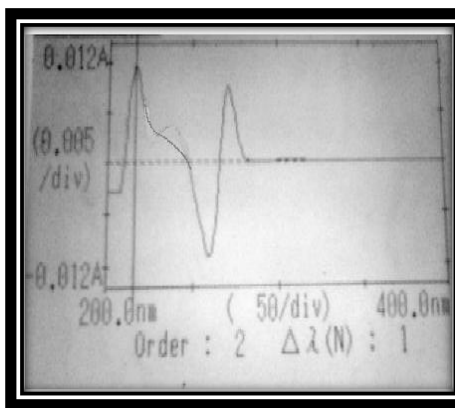


Fig 4: Second order derivative UV spectrum Fig 5: Third order derivative UV spectrum

3. RESULTS AND DISCUSSION

Validation of method was done as per ICH guidelines.

3.1. Accuracy (Recovery Test)

To study the accuracy of the proposed methods, and to check the interference from excipients used. The mean recoveries were found to be 100.02-100.06, 100.00-100.01, 100.00-100.01, and 100.00-100.02 % respectively for UV, first, second, and third derivative spectroscopy^{5,7}. ("Table 1")

Table 1: Data of accuracy study

	Level of % recovery	Preanalysed conc. (µg/ml)	Spiked conc. (µg/ml)	Calculated spiked conc. [µg/ml ± S.D] (n = 3)	% R.S.D.	Recovery (%)
UV Calibration	50	30	10	10.11 ± 0.01429	0.12426	100.06
	100	30	20	21.82 ± 0.014299	0.06549	100.05
	150	30	30	32.2 2 ± 0.015821	0.0491	100.02
First derivative	50	30	10	11.09 ± 0.01429	0.12886	100.00
	100	30	20	19.82 ± 0.014299	0.07249	100.01
	150	30	30	30.22 ± 0.015821	0.05235	100.00
Second derivative	50	30	10	12.90 ± 0.01527	0.01284	100.00
	100	30	20	22.95 ± 0.01429	0.00575	100.01
	150	30	30	33.15 ± 0.01527	0.0461	100.00
Third derivative	50	30	10	12.05 ± 0.057735	0.47913	100.00
	100	30	20	21.90 ± 0.057735	0.26363	100.02
	150	30	30	32.19 ± 0.038105	0.11838	100.001

3.2. Linearity

Under the experimental conditions described the graph obtained for UV, first, second and third derivative spectra showed linear relationship. Regression analysis using the method of least-squares was made for the slope. The regression equations of calibration curves were $y = 2.2 \times 10^{-3}x + 7.1 \times 10^{-3}$, ($r = 0.997$) for the UV, $y = 1.2 \times 10^{-4}x + 2 \times 10^{-3}$, ($r = 0.998$) for the first, $y = 1 \times 10^{-4}x + 0.00$, ($r = 0.997$) for the second and $y = 1 \times 10^{-4}x + 0.00$, ($r = 0.997$) for the third derivative



spectrophotometric methods, respectively. The range was found to be 10 – 60 µg/ml for UV, first, second and third derivative spectrophotometric methods. The statistical parameters given are the regression equation calculated from the calibration graphs, along with the standard deviations of the slope (S_b).

3.3. Limit of Detection (LOD) and Limit of Quantification (LOQ)

Limit of detection (LOD) and limit of quantitation (LOQ) were determined by using the formula based on the standard deviation of response and the slope. The limit of detection (LOD) and limit of quantification (LOQ) were calculated by using the equations $LOD = 3 \times \sigma / S$ and $LOQ = 10 \times \sigma / S$, where σ is the standard deviation, S is the slope ("Table 2")

3.4. Precision

To determine the precision of the method, meglumine solutions at a concentration of 40, 50, 60 µg/ml were analyzed each in triplicate. Solutions for the standard curves were prepared fresh every day. The methods were found to be precise. The % RSD values for inter day precision studies were found to be 0.0048, 0.0024, 0.0018 and 0.00031 for UV, first, second and third derivative spectroscopy. The % RSD values for intra day precision studies were found to be 0.00768, 0.00075, 0.01355 and 0.0046 for UV, first, second and third derivative spectroscopy, respectively. The developed methods are accurate, sensitive and precise for determination of meglumine in bulk.

Table 2: Statistical Data for Calibration Curves for Determination of Meglumine

Parameter	UV	First derivative	Second derivative	Third derivative
Range (µg/ml)	10 - 60	10 - 60	10 - 60	10 - 60
Slop (b)	$2.2 \times 10x + 7.1x \times 10^{-3}$	$1.2 \times 10^{-4}x + 2 \times 10^{-3}$	$1 \times 10^{-4}x + 0.00$	$1 \times 10^{-4}x + 0.00$
Standard deviation (\pm SD)	3.6×10^{-3}	1.53×10^{-5}	4.65×10^{-5}	4.4×10^{-6}
Correlation coefficient (r)	0.997	0.998	0.997	0.997
LOD	0.5	0.05049	1.5	0.1
LOQ	1.6	0.153	4.6	0.44

4. CONCLUSION

This is the first study investigating utility of calibration curve, first order, second order and third order of derivative UV-spectrophotometric methods for determination of meglumine in bulk. The proposed methods are correct, precise, sensitive and economic and can be used for the routine analysis and quality control of meglumine.

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