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Derivative spectroscopy: Development and validation of new spectroscopic method for the estimation of metadoxine in bulk and solid dosage form

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ABSTRACT

A simple and sensitive spectroscopic method in ultraviolet region was developed and validated for the estimation of Metadoxine in pure and pharmaceutical dosage forms by derivative spectroscopy. The method is based on Metadoxine, showing absorbance at 292, 302, 270 and 314 nm for zero order, first order, second order and third order derivative spectroscopy respectively in distilled water. But regression values with best results were found to be best for third order derivative spectroscopy. The method obeys Beers law in the concentration range of 4 to 40µg/ml. The proposed method is precise, accurate, linear, stable and reproducible and can be extended to the analysis of Metadoxine in bulk and tablet formulations.

Key words: Derivative spectroscopy, Metadoxine, UV spectroscopic, U.V estimation.

INTRODUCTION

Chemically Metadoxine (MDL) is pyridoxol L-2-pyrolidone-5-carboxylate an ion pair that combines pyridoxine and pyrrolidone carboxylate[1]. Metadoxine exerts several actions that are beneficial to patients with alcoholic liver diseases[2]. It increases the clearance of alcohol and acetaldehyde and decreases the damaging effect of free radicals, restores ATP and glutathione levels, reduces steatosis and liver fibrosis[3]. Metadoxine has been estimated by HPLC[4] and HPTLC method[5]. Metadoxine is a drug mainly used in liver disorder and alcoholic liver diseases. Metadoxine addresses the multiple causes and mechanisms involved in the Liver disorder and improves Alcohol metabolism and accelerates the elimination of alcohol from the blood. Metadoxine reduces the toxic effects of alcohol. In hepatic stellate cells, Metadoxine prevents the collagen synthesis & reduces fibrosis and acts as an Antifibrotic agent and is a synthetic antioxidant, provides stronger antioxidant protection[6]. The vast potential of Metadoxine in the treatment of alcoholic liver disorders and even an increasing demand for simple and sensitive method for routine analysis has led to the need for development of simple, accurate, economical and reproducible spectroscopic method for the estimation of Metadoxine in bulk and in Pharmaceutical formulation.

MATERIAL AND METHODS

Instrument

Shimadzu UV 1601 double beam spectrophotometer connected to a computer loaded with Shimadzu UVPC software was used for all the

spectroscopic measurements. The spectral bandwidth was 1 nm and the wavelength scanning speed was 2800 nm min^{-1}

Prepartion of standrad solution and sample solution

A stock solution of 1mg mL-1Metadoxine in water was used. The working solutions were 0.04 mg mL^{-1} prepared by transferring 2.0 mL from respective stock solution to a 50 mL Volumetric flask and completing to volume with water.

Determination of Metadoxine in tablets

Brand name

Metadoxil and Alcoliv (500mg.)

Company name

Micro Labs, Hosur and Sun pharmaceuticals, Jammu respectively.

A total of 20 tablets were accurately weighed and powdered in a mortar. An amount equivalent to 100 mg (129.42mg) was taken and dissolved in 40 ml of water and stirred on magnetic stirrer for five minutes. About 10 ml of water was added and stirred for further 5 minutes. The mixture was transferred to two centrifuge tubes and centrifuged at 1000 rpm for 5 minutes. The supernatant was transferred to a 100 ml volumetric flask through a Whatman No. 40 Filter paper. The residue was washed thrice with water and the combined filtrate was made up to the mark

Table 1: Optical characteristics and statistical data

S.No.	Parameters	Results
1.	Absorption maxima (nm)	314
2.	Beer's law limits (mcg/ml)	4 - 40
3.	Molar extinction coefficient (mole-1 cm-1)	0.027542
4.	Sandell,s sensitivity (mcg/cm/0.001 absorbance units)	0.0503478
	Regression equation (y) *	0.9996
5.	Slope (b)	0.0198
	Intercept (a)	-0.0316
6.	Coefficient of variance	0.2030994
7.	Standard deviation**	0.0006240

*y = a + bx; when x is the concentration in µg/ml and y is absorbance unit.
**Three replicate samples.

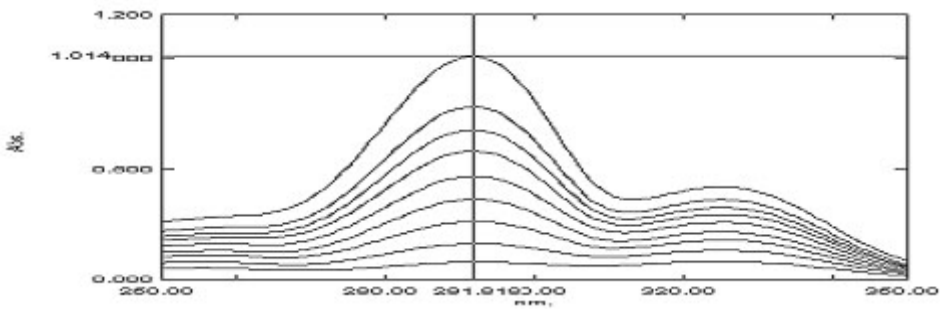

Fig. 1: Zero-order absorption spectra of std. dilutions of MDL in water

Table 2 : Analysis of metadoxin formulation by proposed method

S. No.	Metadoxil solutions (μgmL^{-1})	Conc. of Metadoxil found from zero order method	Conc. of Metadoxil found from first derivative method	Conc. of Metadoxil found from second derivative method	Conc. of Metadoxil found from third derivative method
1.	4	4.228	4.21	4.23	4.01
2.	12	11.79	12.01	12.72	12.05
3.	20	20.96	21.02	20.92	20.09
4.	28	28.001	28.001	27.02	27.06
5.	40	39.95	39.97	39.987	40.01

o Label claim of MDL in each tablet is 500mg.
*Values are average of three determinations. Tablet is metadoxil 500 mg from Micro labs, Hosur.
Result: Average percentage purity of metadoxil was found to be 98.2875 to 104.235 %.

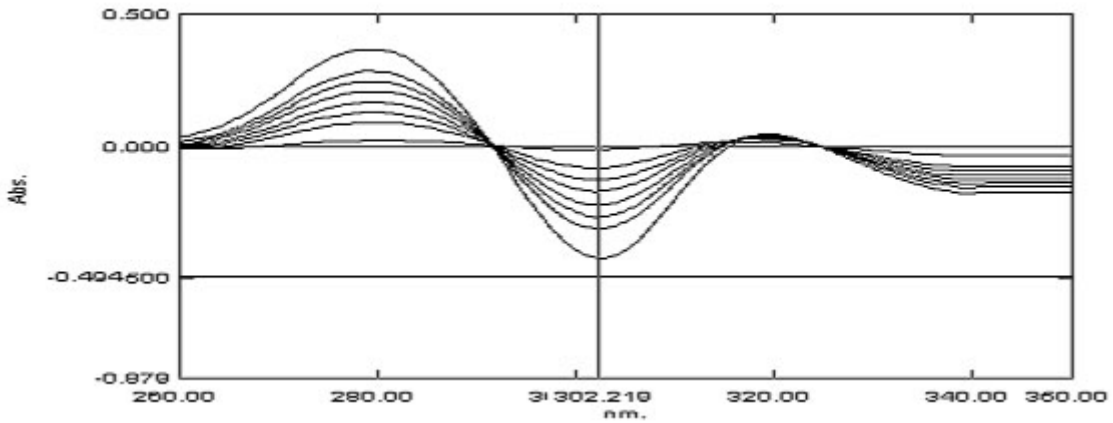

Fig. 2: First derivative spectra of std. dilutions of MDL in water. (Scaling factor = 10 and smoothing factor (δλ) = 10)

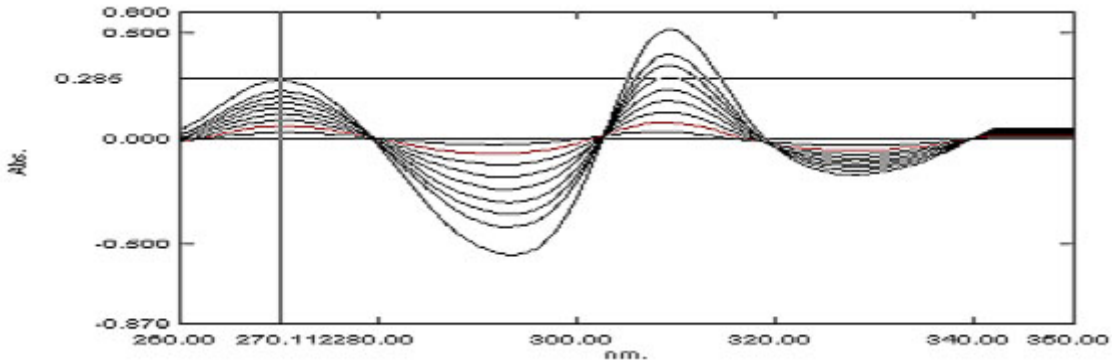

Fig. 3: Second derivative spectra of std. dilutions of MDL in water (Scaling factor = 100 and smoothing factor (δλ) = 10)

Table 3 : Analysis of metadoxin formulation by proposed method

S. No.	Alcolive solution (μgmL^{-1})	Conc. of Alcolive found from zero order method	Conc. of Alcolive found from first derivative method	Conc. of Alcolive found from second derivative method	Conc. of Alcolive found from third derivative method
1.	4	4.26	4.25	4.23	4.11
2.	12	11.73	12.03	12.52	12.13
3.	20	20.91	21.01	20.52	20.12
4.	28	28.011	28.013	27.12	27.13
5.	40	39.98	39.95	39.98	40.11

o Label claim of MDL in each tablet is 500mg.
*Values are average of three determinations. Tablet isAlcolive 500 mg from Sun pharmaceuticals, Jammu
Result: Average percentage purity of metadoxil was found to be 98.1366 to 104.326 %.

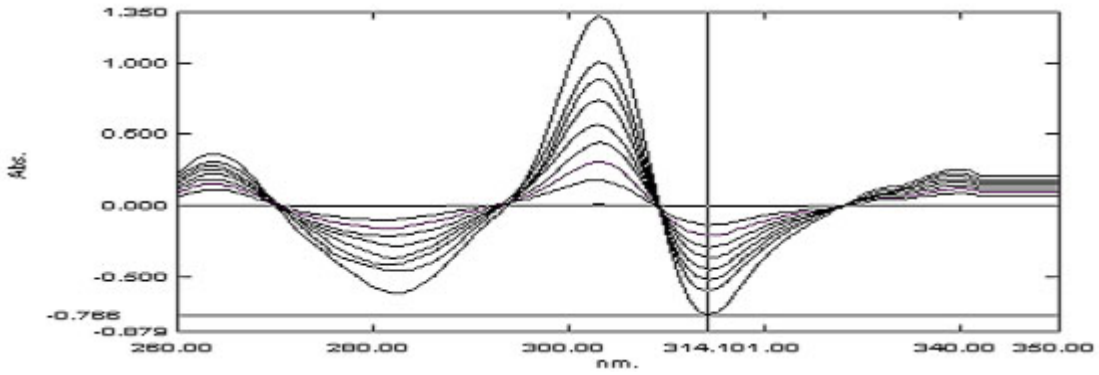

Fig. 4: Third derivative spectra of std. dilutions of MDL in water (Scaling factor = 1000 and smoothing factor (δλ) = 10)

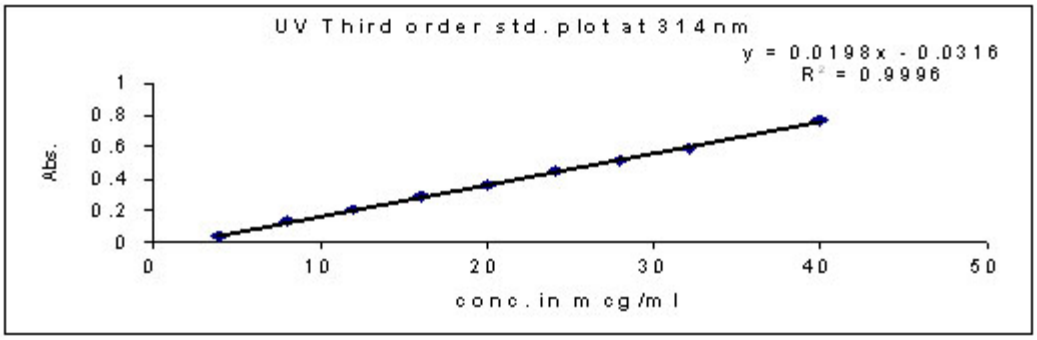

Fig. 5: UV third order std. plot at 314 nm

with water. The sample solution thus prepared was diluted with water to get the solutions containing different concentrations of MDL.

Estimation of metadoxine

An aliquote of test solution (2 ml) was diluted to 100 ml with distilled water. The procedure with standard solution of drug has same concentration as test solution. The absorbance of test and standard solutions were measured at 292, 302, 270, 314 nm against reagent blank. This experiment was repeated three times for bulk drug and formulation and we get three spectra at different wavelengths (292, 302, 270, 314 nm respectively) given in fig. 1-4 with optical activity given in table 1.

RESULTS AND DISCUSSION

In the present study attempts shall be made to develop specific spectroscopic method for the estimation of Metadoxine in bulk and in Pharmaceutical formulation (Tablets).The method involves UV spectroscopic estimation of Metadoxine using distilled water as solvent in bulk and in formulation. The absorption maximum was measured at 314 nm and calibration curve was plotted with linearity in the concentration range 4-40µg/ml.The sandells sensitivity was found out to be 0.0503478 mcg/cm^2 0.001 absorbance units and molar absortivity 0.027542 mol^{-1} cm^{-1}. The regression equation for the proposed method is calculated by Least Square method as Y= a + bx where x is the concentration of the substance in µg and Y is absorbance at specific λ max, -0.0316 is the intercept (a) of the linear line and 0.0198 is the slope (b) of the line. The standard deviation of 0.9996 indicated accuracy and reproducibility of the method. The method was extended for the determination of Metadoxine in tablet formulation. It was observed that the recovery was found to be 99.00 to 101.00% indicating practically no interference of formulation excipients with the proposed method. In the series of 10 different 10 ml volumetric flasks, add 4, 8, 12, 16, 20, 24, 28, 32, 36, 40 µgmL^{-1} of MDL solution were made with distilled water. The solution was scanned and measured at different wavelengths i.e. 292 nm, 302 nm, 270 nm and 314 nm for zero, first, second and third order respectively, because of their lower RSD values. Since the Regression values were found to be best with 3rd order Derivatives, (0.9996) at 314nm, when compare with Zero order derivatives, (0.9949) at 292nm, 1st order derivatives (0.9965) at 302nm. and 2nd order derivatives, (0.9992) at 270nm. respectively and also the accuracy, precision and recovery studies proves that the 3rd order is the best for further analysis of the drug. So the developed spectroscopic methods were found to be simple, accurate, economical and reproducible for the estimation of Metadoxine in bulk and in Pharmaceutical formulation (Tablets).

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