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

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ABSTRACT

Chemically metadoxine is pyridoxol L-2-pyrrolidone-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 increase the clearance of alcohol and acetaldehyde and decreases the damaging effect of free radicals, restores ATP and glutathione levels, reduces steatosis and prevents liver fibrosis[3]. After thorough survey of literature it is found that Metadoxine has been estimated by HPLC[4] and HPTLC[5] methods, but no spectrophotometric methods are cited in the literature, we report simple and sensitive colorimetric method in visible region for the estimation of Metadoxine in pure and pharmaceutical dosage forms by derivative spectroscopy.

KEYWORDS

Derivative spectroscopy;
Metadoxine;
Colorimetric estimation;
FeNO3.

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]. The drug mainly used in liver disorder and alcoholic liver diseases. In hepatic stellate cells, Metadoxine prevents the collagen synthesis and 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.

EXPERIMENTAL

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 1nm and the

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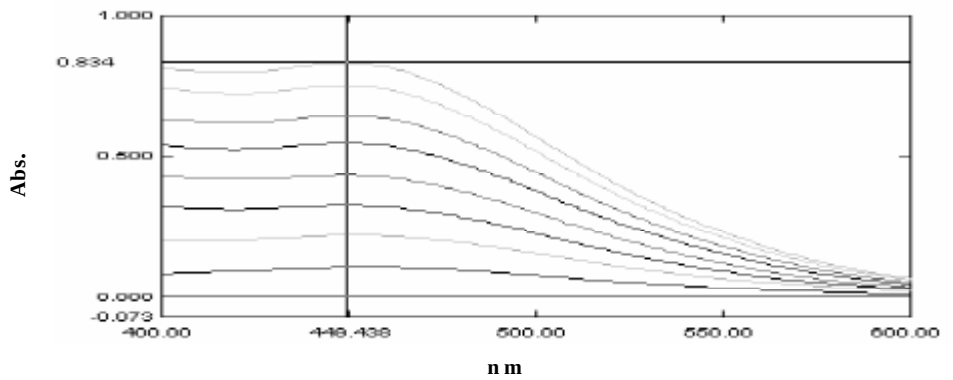

Figure 1 : Showing zero-order overlay absorption spectra and λmax (449nm) of various concentrations of MDL. Conclusion:After scanning the solution in the visible region (400 to 600nm.) the absorption maxima was found to be 449nm which is shown in the graph

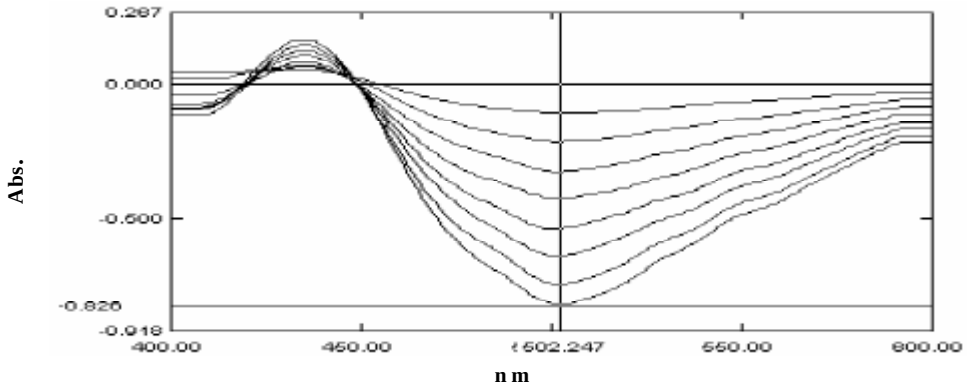

Figure 2: Showing first-order overlay absorption spectra and minimum (502nm) of various concentrations of MDL Conclusion: After scanning the solution in the visible region (400 to 600nm.) the absorption maxima was found to be 502nm which is shown in the graph

wavelength scanning speed was 2800nm min^{-1} A Visible spectrophotometric method has been developed for the estimation of Metadoxine in bulk drug and in tablet formulation. Metadoxine is taken in distilled water with Ferric nitrate reagent and absorbance was measured at 449 and 502nm.

The stock a solution of 1mg mL-1 MDL in water was used. The working solutions were 0.3mg mL^{-1} prepared by transferring 30.0mL from respective stock solution to a 100mL measuring flask and completing to volume with water. Metadoxine was kindly supplied by Micro Labs Limited, India and was certified to be 99.8% pure. The drug was used without further purification. Ferric nitrate reagent (1.5%) was prepared freshly every day during method development. All the solvents and reagents used in spectrophotometric analysis were of analytical reagent grade. Metadoxil tablets of Micro Labs claimed to contain 500mg of Metadoxine was used in analysis. Metadoxil and Alcoliv (500mg.) obtained gift from Micro Labs, Hosur and Sun pharmaceuticals, Jammu respectively. Twenty tablets each containing of 500mg of Metadoxine were weighed, powdered and the tablet powder equivalent to 300mg (388.26mg) of Metadoxine was transferred into 100ml volumetric flask dissolved in 40ml of water and stirred on magnetic stirrer for five minutes. About 10ml 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 with water. The sample solution thus prepared was diluted with water to get the solutions containing different concentrations of Metadoxine.

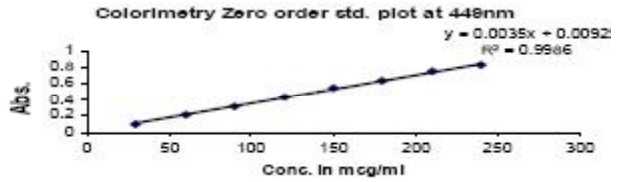

Figure 3 : Calibration curve of metadoxine in distilled water with ferric nitrate reagent for zero order

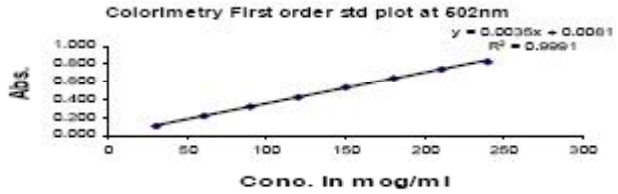

Figure 4 : Calibration curve of metadoxine in distilled water with ferric nitrate reagent for first order

RESULTS AND DISCUSSION

In the present study attempts shall be made to develop specific visible spectroscopic method for the estimation of Metadoxine in bulk and in Pharmaceutical formulation (Tablets).The method involves Colorimetric estimation of Metadoxine using Ferric nitrate reagent with distilled water as solvent in bulk as well as formulation. The absorption maximum was measured at 449 and 502 nmand calibration curve was plotted with linearity in the concentration range 30-300µg/ml(Figures 3 and 4).The sandells sensitivity was found out to be 0.2797163mcg/cm^2 0.001 absorbance units and molar absortivity 0.0035761mol^{-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, 0.0081 is the intercept (a) of the linear line and 0.0035 is the slope (b) of the line(TABLE 1). The standard deviation of 0.9991 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% (TABLES 2 and 3) indicating practically no interference of formulation excipients with the proposed method.

TABLE 1: Optical characteristic of proposed method

S. no.	Parameters	Results
1	Absorption maxima (nm)	502
2	Beer's law limits (mcg/ml)	30 - 300
3	Molar extinction coefficient (mole^{-1} cm^{-1})	0.0035761
4	Sandell,s sensitivity (mcg/cm/0.001 absorbance units)	0.2797163
5	Regression equation (y) *	0.9991
	Slope (b)	0.0035
	Intercept (a)	0.0081
6	Coefficient of variance	0.1833218
7	Standard deviation**	0.000577

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

TABLE 2: Analysis of metadoxin formulation by proposed method

Sl. no.	Concentration of metadoxine in µg mL^{-1}	Ferric nitrate reagent (1.5%)ml	Amount of metadoxine found in µg mL^{-1} (zero order)	Amount of metadoxine found in µg mL^{-1} (first derivative)	% recovery (zero order)	% recovery (first derivative
1	30	2	30.389	30.12	101.2967	100.4
2	90	2	91.865	90.18	102.0722	100.2
3	150	2	152.36	155.62	101.5733	101.08
4	210	2	208.72	210.78	99.39048	100.3714
5	240	2	239.74	240.52	99.89167	100.2167

Label claim of Metadoxine in each tablet is 500mg, *Values are average of three determinations. Tablet 1 is metadoxil 500 mg from Micro labs, Hosur

TABLE 3: Analysis of metadoxin formulation by proposed method

Sl. no.	Concentration of Metadoxine in µg mL^{-1}	Ferric nitrate reagent (1.5%)ml	Amount of metadoxine found in µg mL^{-1} (zero order)	Amount of Metadoxine found in µg mL^{-1} (first derivative)	% recovery (zero order)	% recovery (first derivative
1	30	2	29.12	30.09	97.06667	100.3
2	90	2	91.06	90.11	101.1778	100.1222
3	150	2	151.96	150.81	101.3067	100.54
4	210	2	207.92	211.18	99.00952	100.5619
5	240	2	242.14	241.01	100.8917	100.4208

Label claim of Metadoxine in each tablet is 500mg, *Values are average of three determinations. Tablet 2 is Alcolive 500 mg from Sun pharmaceuticals, Jammu

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In the series of 10 different 10ml volumetric flasks, add 30, 60, 90, 120, 150, 180, 210, 240, 270, and 300μgmL^{-1} of Metadoxine solution were made with distilled water. The solution was scanned and measured at different wavelengths i.e. 449nm and 502nm for zero and first order respectively (Figures1 and 2), because of their lower RSD values. Since the regression values were found to be best with 1st order Derivatives when compare with Zero order derivatives and also the accuracy, precision and recovery studies proves that the 1st order is the best for further analysis of the drug. So the developed Colorimetric method was found to be simple, accurate, economical and reproducible for the estimation of Metadoxine in bulk and in pharmaceutical formulation (Tablets). The R^2 value at zero order and first order was found to be 0.9986 and 0.9991 respectively. The average percentage purity of Metadoxil and Alcolive was found to be near about 98.1734% to 102.0722%.

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