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NOTE

Spectrophotometric Estimation of Metadoxine in Oral Solid Dosage Forms

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Three new, simple sensitive and reproducible spectrophotometric methods have been developed for the estimation of metadoxine in oral solid dosage form, (method **A**, **B** and **C**). Method **A** obeys Beer's law in concentration ranging from 8-64 µg/mL and exhibiting maximum absorption at 291 nm. Method **B** obeys Beer's law in the same concentration from 8-64 µg/mL. By derivatising the primary spectra the second derivative spectrum is obtained. Method **C** is difference spectroscopy method which is based on shifting the λ_{max} by changing the pH of the solution, by adding 0.1 M HCl and 0.1 M NaOH. This produces maximum absorption at 309, 245 and 290 nm. At 245 nm, it obeys Beer's linearity in concentration ranging from 8-64 µg/mL. The methods were extended upto pharmaceutical formulations and there was no interference from any common excipients and diluents. The results of analysis have been validated statistically by recovery studies.

Key Words: Metadoxine, Spectrophotometric determination.

Metadoxine designated chemically as 5-oxo-L-proline compound with 5-hydroxy-6-methyl pyridine-3,4-dimethanol (1:1) with the empirical formula $C_{13}H_{18}N_2O_6$ is useful in preventing the damage produced in early stages of liver disease as it prevents the redox imbalance of the hepatocytes and also prevents TNF-induction in the earliest events of hepatic damage. No method of estimation for metadoxine in formulations has been reported so far except an HPLC method of estimation of the drug in biological fluids[1-3].

All the measurements were made using Shimadzu UV-Visible spectrophotometer with 1 mm matched quartz cells. Metadoxine was obtained as a gift sample from Micro Labs, Bangalore and formulation purchased from the local market of analytical grade. All the solutions were freshly prepared with distilled water, 0.1 M HCl, 0.1 M NaOH.

Standard stock solution: An accurately weighed amount of 100 mg of metadoxine, in 100 mL standard flask, dissolved in distilled water.

Sample solution: The average weight of 20 tablets of metadoxine was determined and finely powdered. The powder equivalent to 500 mg of metodoxine was taken in 100 mL volumetric flask and dissolved in 100 mL of distilled water. The solution was then filtered, first few mL of the filtrate was discarded and remaining solution was used for the analysis.

Assay procedure

Method A: Aliquot of the standard stock solution was suitably diluted to give a varying concentration ranging from 8-64 µg/mL and the solution was scanned in the UV region between 200-400 nm using distilled water as blank. It was found that metadoxine exhibited an intense maximum absorption at about 291 nm.

Method B: The standard stock solution of metadoxine was suitably diluted to give the various concentration ranging from 8-64 µg/mL.These solutions were scanned from 200-400 nm and the primary absorption spectra was recorded. The primary spectrum was then derivatized for the second order. The amplitude (DL) of long wave peak satellite of the second order curve was measured in mm.

Method C: To 1mL of stock solution in a 25 mL volumetric flask, sufficient amount of 0.1 M HCl was added to make up to the volume and a similar solution is prepared by adding sufficient amount of 0.1 M NaOH. These solutions are scanned between 200-400 nm using respective blanks for determining the absorption maximum. The maximum absorption was observed at about 290 nm for the sample in 0.1 M HCl and 309 and 245 nm for the sample in 0.1 M NaOH. Aliquots of standard stock solution, 8-48 µg/mL was transferred to a series of 25 mL volumetric flasks and made up to volume using 0.1 M HCl and 0.1 M NaOH, respectively. The absorbance was measured at 245, 290 and 309 nm, respectively. The difference in absorbance at 245 nm was recorded since it obeys Beer's law.

TABLE-1
OPTICAL CHARACTERISTICS

Parameters	Metadoxine		
	A	B	C
Beer's law limit (µg/mL)	8-64	8-64	8-48
Molar absorptivity (L/mol/cm)	6.003×10^3	-	5.818×10^3
Sandell's sensitivity (µg/mL)	0.05612	-	0.004521
Correlation coefficient	1.008	0.99650.	1.005
Regression equation (y = mx + c)	0.0234x+(-0.08059)	0.2182x+3.106	0.0187x+(-0.0204)
Slope (m)	0.0234	0.2182	0.0187
Intercept (c)	-0.08059	3.1060	-0.0204
Standard deviation (SD)	1.0601	1.5560.	0.8480
Relative standard deviation (RSD)	0.2120	0.3110	0.I697
Limit of detection (LOD)	1.495	2.3735	1.496
Limit of quantification (LOQ]	4.5980	7.131	4.923
Confidence intervals (%)	± 0.1192	± 0.1782	± 0.9660

A = UV Spectrophotometry; B = Derivative spectroscopy; C = Difference spectroscopy.
Mean of three readings.

The optical characteristics such as Beer's law limits, Sandell's sensitivity, molar extinction coefficient, % RSD, regression equation, correlation co-efficient, % range of error, for all the three methods, were calculated and the results are summarized in Table-1.

To evaluate validity and reproducibility of the methods, known amount of pure drug were added to previously analyzed pharmaceutical preparations and the mixtures were analyzed. The proposed methods and the results are presented in Table-2. Interference studies revealed that the common excepients and additives did not interfere. Hence these methods are most economic, simple, sensitive and accurate and can be used for the routine determination of metadoxine in pharmaceutical preparations.

TABLE-2
RESULTS AND RECOVERY STUDY

Drug (Metadoxine)		Label claim (mg)	Amount found by the proposed method (mg)*	Amount of drug added (mg)	Amount recovered (mg)	Percentage recovered
A	Tablet I	500	500.01	10	10.05	100.05
	Tablet II		500.20	20	19.95	99.75
B	Tablet I	500	499.95	20	20.05	100.02
	Tablet II		500.30	10	10.08	100.80
C	Tablet I	500	499.60	20	19.99	99.95
	Tablet II		500.60	10	10.01	100.01

*Mean of three readings.

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