# A REVIEW ON METADOXINE; ANALYTICAL PROFILE AND RECENT ADVANCEMENTS

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# ABSTRACT

Pyridoxine derivative metadoxine has shown great promise as a medicinal agent, especially for the treatment of liver ailments. This article offers a thorough analysis of the pharmacological characteristics of metadoxine, covering its mode of action, recommended uses, and side effects. The paper also discusses the analytical techniques used to quantify metadoxine in a variety of matrices, including biological fluids and pharmaceutical formulations. It is stressed how crucial reliable and precise analytical techniques are for therapeutic medication monitoring, quality assurance, and pharmacokinetic research.

**Keywords:** metadoxine, pharmacological properties, analytical methods, liver diseases, chromatography, mass spectrometry.

# INTRODUCTION

Alcohol intoxication, both acute and chronic, is treated with metadoxine, often referred to as pyridoxine-pyrrolidone carboxylate. Blood alcohol removal from the body is accelerated by metadoxine. The main conditions for which metadoxine is prescribed are fatty liver disease and alcoholism. Alcohol is better metabolized and liver function is enhanced. The possibility of using it to treat cognitive impairment and ADHD has also been studied.

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# Figure-1:Structure of Metadoxine

**Chemical name:** Chemically it is 5-Oxo-L-proline-4, 5-bis (hydroxymethyl)-2- methylpyridin-3-ol

**Chemical formula:** C13H18N2O6

**Molecular weight:** 298.295 g.mol−1

**Category:** Hepatoprotective.

Pyridoxine and pyrrolidone carboxylate (PCA) ion pair salts are combined to form metadoxine. Vitamin B6, pyridoxine, is a precursor of coenzymes that include pyridoxal 5'-phosphate (PLP), which prevents acetaldehyde from inactivating adenosine triphosphate (ATP) and speeds up the metabolism of ethanol. Serotonin (5-HT), epinephrine, norepinephrine, and GABA are four major neurotransmitters that are also produced by pyridoxal phosphate-dependent enzymes.

# Table 1: Spectrophotometric analysis techniques reported in the literature for the determination of metadoxine

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| **Title** | **Method** | **Wavelength** | **Description** | **Reference** |
| Derivative spectroscopy: Development and validation of new spectroscopic method for the estimation of metadoxine in bulk and solid dosage form | UV-Visible spectrophotometric | 292nm for zero order  302nm for first order  270nm for second order  314nm for third order | The proposed method is precise, accurate, linear, stable and reproducible and can be extended to the analysis of Metadoxine in bulk and tablet formulations. | 12 |
| Quantification of metadoxine in pharmaceutical dosage forms by uv-spectrophotometry | UV-Visible spectrophotometric | 291nm | The proposed methods are sensitive, accurate, reproducible and useful for routine determination of metadoxine in pharmaceutical dosage forms | 17 |
| New spectrophotometric methods for estimation of Metadoxine in bulk and pharmaceutical formulations based on redox and oxidative coupling reactions | Spectrophotometric method | Method- 660nm  Method- 460nm | Method A in the concentration range of 5-30 μg/mL  Method B in concentration of 424 μg/mL. | 19 |

**Reported HPLC methods of Metadoxine**

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
| **Title** | **Method** | **Mobile phase** | **Stationary phase** | **Wavelength** | **Reference** |
| Stability-Indicating HPLC Method for the Determination of Metadoxine as Bulk Drug and in Pharmaceutical Dosage Form | HPLC | methanol and water (50: 50, *v/v*). | C18 (5-micron, 25 cm × 4.6 mm, i.d) | 286nm | 9 |
| Determination of metadoxine in human serum by HPLC and its pharmacokinetic studies | HPLC | methanol-5 mmol·L -1 ammonium acetate (14:86, v/v | C18 column (250 mm ×4.6 mm, 5 μm) | 286nm | 8 |
| Pharmacokinetics of metadoxine for injection after repeated doses in healthy volunteers | HPLC | 1:9 (v/v) of acetonitrile- phosphate buffer (pH 7, 0.05 mol/L). | C18 column 125×4 mm (5 µm) | 315nm | 7 |
| Development of RP-HPLC Method for estimation of metadoxine in pharmaceutical formulations. | RP- HPLC | water: methanol 85:15 v/v | C18 column (250 mm length, 4.6 mm internal diameter and 5μm particle size) | 290nm | 6 |
| Application of stability-indicating HPTLC method for quantitative determination of metadoxine in pharmaceutical dosage form | HPTLC | acetone-chloroform-methanol-ammonia (7.0:4.0:3.0:1.2, v/v/v/v) | TLC aluminium plates precoated with silica gel 60F-254 | 315 nm | 13 |
| Method Development and Validation of Metadoxine and Atazanavir in Solid Dosage Form by RP-HPLC | RP-HPLC | Methanol and 5mM Tetra Butyl Ammonium Hydrogen Sulphate (TBHS) 50:50. | C18 RP Column (250 mm x 4.6mm x 5 µm) | 274(Metadoxine), 249( Atazanavir) | 16 |
| Determination of the Related Substances in Metadoxine by HPLC-ELSD | HPLC-ELSD | 0.2 mol·L 1 trifluoroacetic acid-methanol(92∶8) | Agilent Zorbax SB-C18 column(250 mm×4.6 mm,5 μm) | - | 18 |

# CONCLUSION

According to the review's findings, there are numerous spectroscopic and chromatographic methods available for studying a single hepatoprotective ingredient, such metadoxine. It was discovered that the majority of chromatographic methods included a mobile phase consisting of acetonitrile, methanol, water, and ammonium acetate to improve resolution. For the chromatographic approach, the flow rate and an appropriate retention period are recorded. Consequently, it has been determined that every procedure is simple, accurate, repeatable, economical, and exact. HPLC was the method most often employed because it provided the best possible sensitivity, reproducibility, dependability, and analysis time.

# ACKNOWLEDGEMENT

I would like to thank Sarojini Naidu Vanitha Pharmacy Maha Vidyalaya for continuous support

# REFERENCES

# <https://en.wikipedia.org/wiki/Metadoxine>.

1. Metadoxine, Indian Pharmacopoeia 2022 9th edition vol 2 pg 2873-2874.
2. Mirijello A, Sestito L, Antonelli M, Gasbarrini A, Addolorato G. Identification and management of acute alcohol intoxication. European Journal of Internal Medicine **2023,** 108:1-8. <https://doi.org/10.1016/j.ejim.2022.08.013>.
3. Suresh Babu K, Paradesi D. Investigation of Related Impurities in Metadoxine by a Reversed Phase High Performance Liquid Chromatography Technique. Analytical Sciences **2021,** 37(4):581-584. <https://doi.org/10.2116/analsci.20p271>
4. Sneha Lakshmi RP. A Review on Chromatography with High Performance Liquid Chromatography (HPLC) and its Functions. Research and Reviews: Journal of Pharmaceutical Analysis**2015,** 4(1): 1-15.
5. Rajasekhar Reddy D, Azizunissa, Venkatesh S, Gananadhamu S. Development of RP-HPLC Method for Estimation of Metadoxine in PharmaceuticalFormulations. Journal of Innovative Trends in Pharmaceutical Sciences**2010,** 1(1): 64-68.
6. Lü Y, Kang ZS, Liu Y, Li TY, Xiao YH. Pharmacokinetics of metadoxine for injection after repeated doses in healthy volunteers. Chinese Medical Journal **2007,** 120 (2):166-168.
7. YUAN Gui-yan, WANG Ben-jie, WEI Chun-min, GUO Rui-chen. Determination of metadoxine in human serum by HPLC and its pharmacokinetic studies. Chinese Journal of Clinical Pharmacology and Therapeutics**2006,** 11(4): 440-443. <https://manu41.magtech.com.cn/Jweb_clyl/EN/Y2006/V11/I4/440>
8. Kaul N, Agrawal H, Patil B, Kakad A, Dhaneshwar SR. Stability-Indicating HPLC Method for the Determination of Metadoxine as Bulk Drug and in Pharmaceutical Dosage Form. Chromatographia**2004,** 60: 501–510. <https://doi.org/10.1365/s10337-004-0429-z>

# Shpilenya LS, Muzychenko AP, Gasbarrini G, Addolorato G. Metadoxine in acute alcohol intoxication:a double blind, randomized, placebo-controlled study[J].Alcohol Clin Exp Res, 2002;26:340-6

# DiazMMC, DiazMA, Villamil SV, Cruz FC.Efficacy of metadoxine in the management of acute alcohol intoxication[J].J Int Med Res, 2002;30:44-51

# P. Kumar1, D.S. Mittan3, A. Malik2, N. Kaushik2, A. Kushnoor2 and N. Derivative spectroscopy: Development and validation of new spectroscopic method for the estimation of metadoxine in bulk and solid dosage form. Oriental Journal of Chemistry Vol. 24(1), 313-317 (2008).

# Neeraj Kaul, Himani Agarwal, Bharat patil, Abhijit kakad,S.R.Dhaneshwar. Application of stability indicating HPTLC method for quantitative determination of metadoxine in pharmaceutical dosage form.Il Farmaco,2005 volume60,Pages 351-360

# Pradeep kumar\*, Dhirender singh mittan, Anuj malik¹, Niranjan kaushik¹, Ashok kushnoor¹ and Nagaraj gowda. Derivative spectroscopy: Development and validation of new spectroscopic method for the estimation of metadoxine in bulk and solid dosage form. Oriental Journal of Chemistry, Vol. 24(1), 313-317 (2008).

# Lorenzo Leggio, George A. Kenna, Anna Ferrulli, William H. Zywiak, Fabio Caputo, Robert M. Swift, Giovanni Addolorato. Preliminary findings on the use of metadoxine for the treatment of alcohol dependence and alcoholic liver disease. Human Psychopharmacology 16 November 2011

# Upender Rao Eslawath\*, Rajashekar Vadlakonda1, Thandra Yakaiah2\*. Method Development and Validation of Metadoxine and Atazanavir in Solid Dosage Form by RP-HPLC. IJSRM July 2017 Vol.:7, Issue: 1.

# [V. Venugopal](https://www.semanticscholar.org/author/V.-Venugopal/2076298445), [B. Arun](https://www.semanticscholar.org/author/B.-Arun/83294734), [T. Mahati](https://www.semanticscholar.org/author/T.-Mahati/98160473), [R. Himaja](https://www.semanticscholar.org/author/R.-Himaja/97769710), [T. Kavitha](https://www.semanticscholar.org/author/T.-Kavitha/2102108174). Quantification of metadoxine in pharmaceutical dosage forms by uv-spectrophotometry semantic scholar 2011

# Y. Wei-feng, Lin Yi. Determination of the Related Substances in Metadoxine by HPLC-ELSD.2012

# A. Unnisa, Rajasekhar Dirisala, S. Gananathamu. New spectrophotometric methods for estimation of metadoxine in bulk and pharmaceutical formulations based on redox and oxidative coupling reactions. Chemistry medicine.2011.

# 