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A Review on Analytical Methods for Estimation of Mementine Hydrochloride in Pharmaceutical Dosage Form

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ABSTRACT
Memantine is an Alzheimer's disease medicine that helps to decrease the course of the illness. It is administered orally. Headache, constipation, drowsiness, and dizziness are all common adverse effects. Blood clots, insanity, and heart failure are all possible severe adverse effects. It is thought to function by inhibiting NMDA receptors. In 2003, the FDA authorised memantine for medicinal use in the United States. It can be purchased as a generic drug. With almost 3 million prescriptions written in 2019, it was the 169th most widely prescribed drug in the United States. Analytical processes are crucial when it comes to developing solutions. This article will provide an overview and classification of the many analytical methodologies used to identify supply concernspharmaceutical analysis serves a unique role in the quality assurance and internal control of most pharmaceutical drugs and preparations. The rapid expansion of the pharmaceutical and pharmaceutical industries in many parts of the world has resulted in an increase in demand for new analytical methods in the pharmaceutical industry. As a result, honing analytical skills has become a worthwhile learning experience. Recent breakthroughs in analytical methods have emerged from advancements in analytical instruments.

KEYWORDS Introduction of Memantine, Pharm acology, Pharmacokinetics, HPLC Method.

I. INTRODUCTION

Memantine is an NMDA receptor antagonist that is used to treat mild to moderate Alzheimer's disease.

Memantine is an N-methyl-D-aspartate (NMDA) receptor antagonist that was first licenced by the FDA in 2013. It is used to treat Alzheimer's disease (AD). It differs from many other Alzheimer's Illness drugs in that it operates through a different method than the cholinesterase enzyme inhibitors often used to treat the disease. 2. Memantine inhibits the effects of glutamate, a neurotransmitter that causes neuronal excitability and overstimulation in Alzheimer's disease. [8]

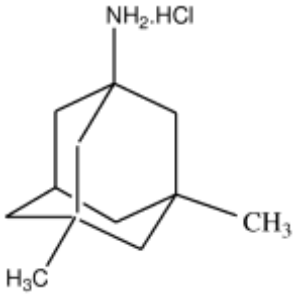

Fig. 1. Structure of Memantine Hydrochloride

DRUG PROFILE:

Drug	Memantine Hydrochloride
IUPAC Name	3,5-dimethyladamantan-1-amine hydrochloride
Chemical Formula	$C_{12}H_{22}ClN$
Molecular Mass	215.76
Solubility	Soluble in water (100 mM), DMSO (43 mg/ml at 25° C), and ethanol (43 mg/ml at 25° C).
pKa	10.7
Melting Point	258^0C

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Therapeutic Use	Memantine is an NMDA receptor antagonist used to treat moderate to severe dementia in Alzheimer's.

PHARMACOLOGY [12,13]

Indication : Memantine is a medication used to treat moderate to severe Alzheimer's disease. According to a more recent systemic review and meta-analysis 6, memantine is effective as a first-line therapy for Alzheimer's dementia. Cholinesterase inhibitors might be used with memantine to improve behavioural problems and other dementia symptoms.

Pharmacodynamics : This medicine prevents calcium influx into cells, which is generally mediated by glutamate-induced prolonged NMDA receptor activation. As a result, Alzheimer's dementia symptoms improve, as evidenced by improved cognition and other positive central nervous system benefits.

Mechanism of action : Some Alzheimer's disease symptoms are considered to be mediated by glutamate-induced activation of the N-methyl-D-aspartate (NMDA) receptors in the central nervous system. Due to glutamate's excitatory qualities, this overactivation is hypothesised to lead to neurotoxicity. Memantine's pharmacological activity is likely due to its nature as an uncompetitive (open-channel) NMDA receptor antagonist, which prevents glutamate activation on this receptor. Memantine prefers cation channels controlled by the NMDA receptor. Despite these antagonistic effects, memantine has not been shown to prevent or delay neurodegeneration in Alzheimer's disease patients.

Pharmacokinetic :

Absorption : Memantine is well absorbed after an oral dosage. It takes 3-7 hours to reach peak medication concentrations. When taken at standard therapeutic levels, memantine has a linear pharmacokinetic profile. Meals has no effect on the absorption of memantine, therefore it can be taken with or without food.**Volume of distribution :** Memantine's average distribution volume is 9-11 L/kg.**Metabolism :** In the liver, this medication is partly metabolised. The hepatic CYP450 enzyme system has a minor role in this drug's metabolism. **Route of elimination :** The majority of this medicine is eliminated in the urine. Approximately 48% of memantine given is excreted unaltered in the urine.

The remaining medication is broken down into three major metabolites. The N-glucuronide conjugate, 6-hydroxy memantine, and 1-nitroso-deaminated memantine are the three metabolites that have limited NMDA receptor antagonist action.

II. LITERATURE REVIEW

1. **Tukaram B Sawant, Dhananjay V Mane-** Using high performance liquid chromatography with a refractive index (RI) detector, design and verify a chromatographic technique to quantify the quantity of drug (assay) in tablets of memantine hydrochloride (MEM). Methods: The chromatographic separation was performed using an isocratic mobile phase consisting of buffer (pH-6.0): Methanol (45:55 v/v) injected at a flow rate of 1.0 ml/min on a C18 (250 4.5 mm, 5) column. A RI detector was used to check effluent detection. Conclusion: The approach was discovered to be simple, commercial, precise, accurate, and robust, and it can be used to determine MEM assay in tablets and capsules.
2. **Sergio del Rio-Sancho, César E. Serna-Jiménez-** The goal of this study was to verify an accurate and exact high-performance liquid chromatography (HPLC) technique for the quantitative measurement of memantine hydrochloride using UV detection. It was essential to extract the medication and execute a dansylation procedure that permitted UV/visible detection of the derivatized molecule in order to examine a molecule with no chromophoric groups that could be recognised by a UV/visible detector. A 150 mm Kromasil C18 column was used to separate the samples at room temperature. In the concentration range of 0.5 to 50 g/mL, the detection response at 218 nm was found to be linear. Specficity, linearity, precision, accuracy, limit of detection, limit of quantification, and resilience were all tested. The detection limit (LOD) was 0.144 g/mL, while the quantification limit (LOQ) was 0.437 g/mL. In all of the settings tested, the dansylated memantine complex remained stable for at least five days. The measurement of memantine hydrochloride present in samples from a study of its in vitro transdermal penetration confirmed the method's potential application.
3. **Bhavil Narola, A.S. Singh-** The invention and validation of a stability-indicating high-performance liquid chromatographic technique

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for the quantitative detection of Memantine hydrochloride is the subject of this research. Memantine hydrochloride was derivatized with 0.015 M 9-fluorenylmethyl chloroformate (FMOC) and 0.5 M borate buffer solution at room temperature for 20 minutes, and chromatographic separation was achieved by injecting 10 L of the derivatized mixture into a Waters HPLC system with photodiode array detector and a kromasil C18 column (150 4.6 mm), 5 The mobile phase contains 80% acetonitrile and 20% phosphate buffer solution, with a flow rate of 2 millilitres per minute. It took around 7.5 minutes to elute the Memantine.The volume of FMOC utilised in derivatization, as well as the concentration and duration of derivatization, were optimised and employed. On a bulk sample of Memantine hydrochloride, forced degradation investigations were carried out utilising acid (5.0 N hydrochloric acid), base (1.0 N sodium hydroxide), oxidation (30 percent hydrogen peroxide), thermal (105°C), photolytic, and humidity conditions. The devised LC technique was tested for specificity, accuracy (percent RSD about 0.70 percent), linearity (range about 70–130 g/mL), ruggedness (overall percent RSD about 0.35 percent), stability in analytical solution (Cumulative percent RSD about 0.11 percent after 1450 minutes), and robustness.

4. **Syeda noorain amena, s. H. Rizwan** - To design and test a stability indicating technique for Memantine HCl and Donepezil HCl analyses. Methods: The chromatographic separation was carried out using a Hypersil BDS (4.6 x 150 mm, 5) with Sodium dihydrogen ortho phosphate: Acetonitrile (30:70v/v) at a flow rate of 1 ml/min and UV Detector detection of both eluents. Results: Memantine HCl and Donepezil HCl had retention times of 2.833 and 4.777 minutes, respectively. Over the range of 40-120g/ml for Memantine HCl and 20-60g/ml for Donepezil HCl, the method was shown to be linear. Memantine HCl and Donepezil HCl were reported to have 99.62 percent and 99.45 percent recovery, respectively.Memantine HCl and Donepezil HCl have a purity of 98.5 percent and 98.6 percent, respectively. Memantine HCl and Donepezil HCl have a limit of detection of 3.69 g/ml and 2.72 g/ml, respectively, and a limit of quantification of 11.13 g/ml and 8.25 g/ml, respectively. Memantine HCl and Donepezil HCl exhibited no degradation in acid (0.1M HCl), base (0.1M NaOH), peroxide, heat, or sunshine in stress degradation experiments. Conclusion: For the detection of Memantine HCl and Donepezil HCl, a novel sensitive, simple, and stable indicating high performance layer chromatographic (HPLC) technique has been developed and validated. The proposed approach may be used to determine the stability of Memantine HCl and Donepezil HCl on a regular basis.
5. **Patel KH, Patel SK, Karkhanis VV and Captain AD** - We developed and verified an accurate HPTLC analytical technique for estimating Memantine Hydrochloride. The NMDA receptor antagonist memantine hydrochloride is frequently used to treat Alzheimer's disease. Aluminum plates pre-coated with silica gel G60F254 as a stationary phase and n-Hexane: Ethyl acetate: Diethylamine (5:5:0.7 percent v/v/v) as a mobile phase were used to create the HPTLC technique. After immersing the isolated spots in Dragendorff's reagent solution, they appeared as orange spots. According to the ICH Guideline, the approach was determined to be Linear, Accurate, Precise, and Robust. For Memantine HCl, linearity was determined to be 5000-30000 ng/band. For Memantine HCl, the LOD and LOQ were determined to be 80.07ng/band and 242.637ng/band, respectively. As a result, the established method may be used to calculate Memantine Hydrochloride.
6. **Tukaram B. Sawant, Vikas S. Wakchaure** - The goal of this work was to use high-performance liquid chromatography with a refractive index (RI) detector to create an analytical technique for quantifying memantine (MEM) hydrochloride in dissolution samples. The chromatographic separation was performed using an isocratic mobile phase of buffer (pH 5.2):methanol (40:60 v/v) injected at a flow rate of 1.0 mL/min on a C18 (250 4.5 mm, 5 m) column. The RI detector was used to monitor the column effluents. MEM's retention time was determined to be 6.5 0.3 minutes. The devised chromatographic technique was verified and shown to be linear for MEM concentrations between 5.0 and 45.0 g/mL. MEM recovery was determined to be 99.2 0.5 percent (w/w) on average.The approach was discovered to be simple, quick, exact, and accurate, and it may be used to quantify MEM in dissolving samples.

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Sr. No.	Authors	Method	Description	Reference
1	**Tukaram B Sawant, Dhananjay V Mane**	RP- HPLC method	**Column :** C18 column (250 × 4.6 mm, id, 5µ) **M.P :**buffer (pH-6.0): Methanol (45:55 v/v) **F.R :** 1.0 ml/min **Linearity :**50-150 µg/ml **R.T. :**7 min	1
2	**Sergio del Rio-Sancho, César E. Serna-Jiménez**	UV- HPLC method	**Column :** Kromasil C-18, 4.5µm column (250mm x 4.6 mm, 5m) **M.P :** hydrochloric acid water solution (0.01 M; pH 2.4)-methanol (15 : 85, v/v) **F.R :** 1.2 ml/min **Linearity :** 0.5-50 µg/ml **Lambda max :** 218 nm **R.T. :** 5.5 min	2
3	**Bhavil Narola, A.S. Singh**	Stability Indicating HPLC method	**Column :** kromasil BDS C18 250mm×4.6mm× 5µm **M.P :**0.05 Molar (M) borate buffer pH 8.5 : acetonitrile [50:50] (v/v) **F.R :** 2.0 ml/min **Linearity :** 70-130 µg/ml **Lambda max :** 265 nm **R.T. :** 7.5 min	3
4	**Syeda noorain amena, S. H. Rizwan**	Stability Indicating HPLC method	**Column :** Hypercil BDS C18 250mm×4.6mm× 5µm **M.P :** Sodium dihydrogen ortho phosphate : Acetonitrile (30:70v/v) **F.R :** 1.0 ml/min **Linearity :** 40-120 µg/ml **Lambda max :** 271 nm **R.T. :** 2.833 min	4
5	**Patel KH, Patel SK, Karkhanis VV and Captain AD**	HPTLC method	**M.P :**n-Hexane: Ethyl acetate: Diethylamine (5:5:0.7 % v/v/v) **Linearity :**5000-30000 ng/band	5
6	**Tukaram B. Sawant, Vikas S. Wakchaure**	HPLC with RI detector	**Column :** C18 column (250mm x 4.6 mm, 5m) **M.P :**buffer (pH 5.2):methanol (40:60 v/v) **F.R :** 1.0 ml/min **Linearity :**5-45 µg/ml **R.T. :**6.5 min	6
7	**Hassan jalalizadeh , mahdi raei**	Stability Indicating HPLC method	**Column :** Novapak BDS C18 250mm×4.6mm× 5µm **M.P :** acetonitrile and sodium dihydrogen phosphate (pH 2.5; 0.05	7

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			M) (70: 30, v/v) **Linearity :** 1-12 µg/ml **Lambda max :** 360 nm	

Validation Parameter:[8-11]

Validation is an essential component of every successful analytical technique. The method used for a particular test is appropriate for the situation. The validation method is used to check the quality, reliability, and consistency of analytical results by validating that the analytical method is applied. The United States Patent and Trademark Office (USPTO) has released an eight-step method validation procedure:

1. Accuracy:
2. Precision
3. Specificity
4. Linearity
5. Range
6. Detection limit
7. Quantitation limit
8. Robusteness
9. Ruggedness
10. Sensitivity
11. Repeatability
12. Reproducibility

III. CONCLUSION

This research classifies a new fast, accurate, and exact analytical method for measuring Memantine HCL in most and unknown amounts of pharmaceutical goods. The aforementioned study includes analytical procedures for analysing Memantine bulk and tablet dosage forms. According to a survey of the literature, several techniques to the production and validation of various drugs have been reported. The different analytical techniques used to analyse Memantine are discussed in this study. The use of HPLC, UPLC, bulk LC-MS/MS, and medicinal dose forms has all been investigated. These methods have been discussed in relation to medication development and validation.

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