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DEVELOPMENT AND VALIDATION OF RP-UPLC METHOD FOR THE SIMULTANEOUS ESTIMATION OF MEMANTINE AND DONEPEZIL IN BULK AND PHARMACEUTICAL DOSAGE FORMS

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ABSTRACT

A rapid and reliable RP-UPLC method was developed for the simultaneous estimation of Memantine and Donepezil in bulk drugs and combined dosage forms. Chromatographic separation was carried out on a C18 column (100 mm × 4.6 mm, 3 µm) using Solution A (Buffer:Methanol, 70:30, v/v) and Solution B (Acetonitrile:Methanol:Water, 90:5:5, v/v) as the mobile phase at a column temperature of 30°C. Detection was performed at 257 nm. Memantine and Donepezil showed retention times of 1.175 min and 1.666 min, respectively. System suitability results were within acceptable limits, with %RSD values of 0.65 and 0.80. The method exhibited excellent linearity (R^2 = 0.9995 and 0.9999) and high accuracy with recoveries between 98.87–100.05%. Stress degradation studies indicated that both drugs were stable under acidic, alkaline, oxidative, thermal, photolytic, and neutral conditions, confirming the method as stability-indicating. The proposed RP-UPLC method is simple, fast, robust, and validated as per ICH guidelines, making it suitable for routine quality-control analysis of Memantine and Donepezil.

KEYWORDS: Memantine, Donepezil, RP-UPLC, Linearity, Accuracy, Precision, Stress Degradation.

INTRODUCTION

Alzheimer's disease (AD) is a progressive neurodegenerative disorder characterized by memory loss, cognitive decline, and behavioral disturbances, making it one of the major public health challenges of the 21st century.[1] Current treatment strategies primarily involve acetylcholinesterase inhibitors and NMDA receptor antagonists, which provide symptomatic relief and improve functional outcomes.[2] Donepezil, an acetylcholinesterase inhibitor, is widely used in mild to moderate AD, whereas Memantine, an NMDA receptor antagonist, is recommended for moderate to severe stages.[3,4] These agents are frequently prescribed together because they offer complementary mechanisms of action. Clinical studies demonstrate that combination therapy results in improved cognition, delayed disease progression, and better overall quality of life for patients.[5,6]

To ensure the safety, efficacy, and therapeutic consistency of these drugs, reliable analytical methods are essential. Analytical evaluation plays a crucial role in confirming drug identity, purity, stability, and potency, all of which are critical for regulatory compliance and pharmaceutical quality assurance.[7–9] Although various classical techniques such as titrimetry and spectroscopy are available, their application is limited for complex mixtures. More advanced approaches—including spectrophotometry, chromatography, and hyphenated techniques like LC-MS/MS and GC-MS—provide higher sensitivity and selectivity, making them suitable for modern pharmaceutical analysis.[10,11]

High-Performance Liquid Chromatography (HPLC) has long served as the standard tool for drug quantification. However, conventional HPLC is often limited by longer run times and higher solvent consumption. The evolution of chromatographic science has led to the development of Ultra-Performance Liquid Chromatography (UPLC), which employs sub-2 µm particles and high-pressure systems to deliver faster analysis, improved resolution, enhanced sensitivity, and reduced solvent use.[12,13] The performance advantages of UPLC are strongly supported by the Van Deemter equation, which explains how small particle sizes improve efficiency even at higher flow rates.[14,15]

Although analytical procedures for individual estimation of Memantine and Donepezil exist, only limited work has been reported on their simultaneous determination. Many conventional HPLC methods suffer from longer retention times, inadequate peak separation, or high solvent requirements.[16-18] This creates a clear need for a stability-indicating, rapid, sensitive, and high-resolution RP-UPLC method capable of quantifying both drugs simultaneously in bulk and pharmaceutical dosage forms.

Rationale of the Study

Because Memantine and Donepezil are frequently administered as a combination therapy in Alzheimer's disease, there is a strong requirement for an analytical technique that can estimate both drugs accurately in a single run. UPLC provides distinct advantages over HPLC, including superior resolution, reduced analysis time, lower solvent usage, and improved method robustness.[19-24] With advancements in UPLC instrumentation—such as high-pressure pumps, precise injection systems, and optimized detectors—modern RP-UPLC methods are capable of delivering greater accuracy, sensitivity, and reproducibility.[25–28]

Therefore, the present study focuses on developing and validating a novel RP-UPLC method for the simultaneous estimation of Memantine and Donepezil in bulk and pharmaceutical dosage forms, ensuring high precision, accuracy, rapidity, and suitability for routine quality control as well as stability studies.

Drug Profiles

Memantine[29]

Memantine is an NMDA receptor antagonist widely used for Alzheimer's disease (Navneet et al., 2011). Its properties are summarized in Table 1.

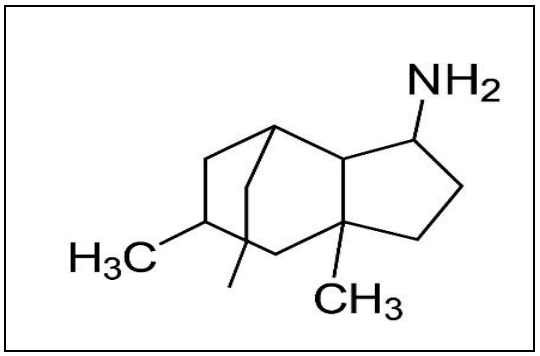


Fig 1: Chemical structure of Memantine.

Table 1: Memantine Profile.

Parameter	Details
Chemical Name	3,5-dimethyladamantan-1-amine
Molecular Formula	$C_{12}H_{21}N$
Molecular Weight	179.3 g/mol
Appearance	Gray solid
pKa	10.7
Solubility	Water, DMSO, ethanol
Category	NMDA receptor antagonist
Dosage Form	Capsules

Donepezil[30]

Donepezil is an acetylcholinesterase inhibitor approved by the USFDA for the management of Alzheimer's disease. It acts as a selective, reversible, and non-competitive inhibitor of acetylcholinesterase.

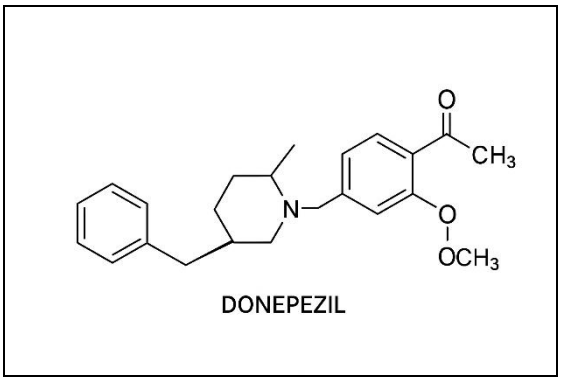


Fig. 2: Chemical structure of Donepezil.

Table 2: Donepezil Profile.

Parameter	Details
Chemical Name	(RS)-2-[(1-Benzyl-4-piperidyl)methyl]-5,6-dimethoxy-2,3-dihydroinden-1-one
Molecular Formula	$C_{24}H_{29}NO_3$
Molecular Weight	379.49 g/mol
Appearance	Pale yellow solid
pKa	8.9
Solubility	Water, methanol, ethanol
Category	Acetylcholinesterase inhibitor
Dosage Form	Capsules

List of drugs used in the study

The drugs used in this study are summarized in Table 3.

Table 3: List of drugs used in the study.

Name of the API	Procured From	Brand Name / Manufacturer	Label Claim
Memantine and Donepezil	Fortune Pharma, Hyderabad	Namzaric / Actavis	Memantine – 14 mg, Donepezil – 10 mg

MATERIALS AND METHODS

Instruments and Equipment Specifications

The study was conducted using an ACQUITY UPLC system equipped with a TUV detector and Empower 2 software for data acquisition.[31] A Digisum Electronics pH meter was used for precise pH measurements, while weighing of chemicals was performed using a SCALETEC electronic balance. Sample sonication was carried out using an ENERTECH ultrasonicator to ensure complete dissolution of the analytes.[32] The selected UPLC system offers high sensitivity and resolution for the simultaneous quantification of Memantine and Donepezil in tablet formulations.[31,32]

Table 4: Instruments used in the study.

Instrument/Equipment	Specification
UPLC	ACQUITY, TUV Detector, Empower 2[1]
pH Meter	Digisum Electronics[2]
Electronic Balance	SCALETEC[2]
Ultra-sonicator	ENERTECH[2]

Chemicals and Reagents

All chemicals and solvents were of analytical or UPLC grade. KH_2PO_4 was obtained from Rankem (AR grade), acetonitrile (HPLC grade) from Merck, and water was purified using a Milli-Q system.[33,34] Memantine and Donepezil reference standards were procured from Fortune Pharma, Hyderabad, and the commercial formulation (Namzaric/Actavis) contained 14 mg Memantine and 10 mg Donepezil.

Chemical/Solvent	Grade
KH_2PO_4	AR
Acetonitrile	UPLC/HPLC grade
Water	Milli-Q (UPLC grade)

Method Development by RP-UPLC

The RP-UPLC method was developed using a systematic trial-and-error approach. Various mobile phase compositions, columns, and flow rates were evaluated to achieve optimal resolution, peak shape, and system suitability parameters.[35–37]

Stock Solution Preparation

Memantine (14 mg) and Donepezil (10 mg) were accurately weighed and dissolved in an appropriate diluent to obtain stock solutions of 140µg/mL and 100 µg/mL, respectively. The stock solutions were used for standard preparation and forced degradation studies.[35]

Standard Solution Preparation

From each stock solution, 1 mL was diluted to 10 mL to obtain working standard solutions of 14 µg/mL Memantine and 10 µg/mL Donepezil, representing 100% assay concentration.[35]

Sample Solution Preparation

Tablet powder equivalent to 14 mg Memantine and 10 mg Donepezil was weighed and diluted to achieve final concentrations matching the standard solutions. This ensures accurate comparison for quantification.[35]

Optimization Trials

Multiple trials were conducted to identify the optimal chromatographic conditions. The choice of column, mobile phase, and flow rate significantly impacted the peak resolution and system suitability parameters.[36,37]

Table 5: Trials for Method Development.

Trial	Column	Mobile Phase	Flow Rate	Observation
1	Hibar C18 (100×2.1 mm, 1.8 µm)	KH_2PO_4 : ACN (60:40)	0.3 mL/min	Peaks poorly resolved
2	BEH C18 (50×2.1 mm, 1.8 µm)	KH_2PO_4 : ACN (70:30)	0.3 mL/min	Broad Donepezil peak, reduced efficiency
3	X Bridge C18 (100×2.1 mm, 1.8 µm)	KH_2PO_4 : ACN (50:50)	0.3 mL/min	Inadequate resolution
4	X Bridge C18 (100×2.1 mm, 1.8 µm)	KH_2PO_4 : ACN (70:30)	0.3 mL/min	Optimized; system suitability parameters acceptable

The final optimized method used X-Bridge C18 column with a mobile phase of 0.1 N KH_2PO_4: ACN (70:30 v/v), flow rate 0.3 mL/min, column temperature 30°C, detection wavelength 257 nm, and injection volume 1 µL.[36,37]

Method Validation

The optimized RP-UPLC method was validated as per ICH Q2(R1) guidelines.[8] System suitability, linearity, accuracy, precision, robustness, specificity, and sensitivity were evaluated. Linearity was established for Memantine (3.5–21 µg/mL) and Donepezil (2.5–15 µg/mL) with R^2 >0.999. Accuracy (% recovery) ranged 98–102%, and precision (%RSD) was <2%. LOD and LOQ were determined using the standard deviation of response method.[38]

Forced Degradation Studies

Stock solutions were subjected to acidic (2N HCl), basic (2N NaOH), oxidative (20% H_2O_2), thermal (105°C/75% RH), photolytic (UV, 7 days), and neutral stress conditions. Chromatograms confirmed the method's stability-indicating capability.[39]

Assay of Commercial Formulation

The % purity of Memantine and Donepezil in commercial tablets was determined using the validated RP-UPLC method. Calculations were performed using standard formulae.[38]

%Assay = (AT / AS) × (WS / DS) × (DT / WT) × (P / 100) × (Avg Wt / Label Claim) × 100

RESULTS AND DISCUSSION

Method Validation

The developed RP-UPLC method was validated as per ICH Q2(R1) guidelines.[8]

System Suitability

Six replicates of standard solutions of Memantine and Donepezil were analyzed. The USP plate count for all analytes was >2000, and wTHE tailing factor was ≤2. %RSD of peak areas was ≤2%, confirming system suitability. Chromatograms are shown in Figures 5.1–5.6, and data are summarized in Tables 6.

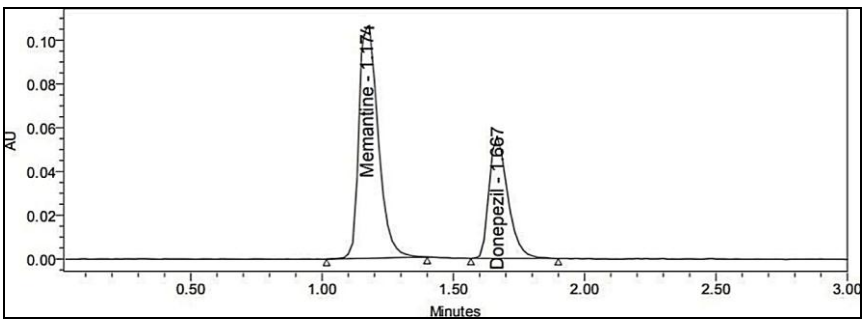


Fig. 3: Representative chromatogram showing well-resolved peaks of Memantine and Donepezil.

Table 6: System Suitability Parameters of Memantine and Donepezil.

Parameter	Memantine (Mean ± SD)	Donepezil (Mean ± SD)	Acceptance Criteria
Retention Time (min)	1.174 ± 0.006	1.666 ± 0.008	Consistent, N > 2000
Peak Area	546457.8 ± 7463.4	366573 ± 2368.5	%RSD ≤ 2
Theoretical Plate Count	3434 ± 196	3889 ± 39	> 2000
Tailing Factor	1.37 ± 0.04	1.37 ± 0.03	0.8–2.0
Resolution	3.58 ± 0.03	3.55 ± 0.08	> 2

Linearity

The method showed excellent linearity with R^2 values of 0.9995 for Memantine (3.5–21 µg/mL) and 0.9999 for Donepezil (2.5–15 µg/mL), in accordance with ICH guidelines (Table 7).

Table 7: Linearity of Memantine and Donepezil.

Memantine				Donepezil	
S No	% Level	Concentration	Peak area	Concentration	Peak area
1	25%	3.5	131454	2.5	94745
2	50%	7	275907	5	184531
3	75%	10.5	415665	7.5	270329
4	100%	14	552758	10	362758
5	125%	17.5	681185	12.5	452811
6	150%	21	811678	15	540424
Correlation Coefficient (R^2)			0.9995		0.9999

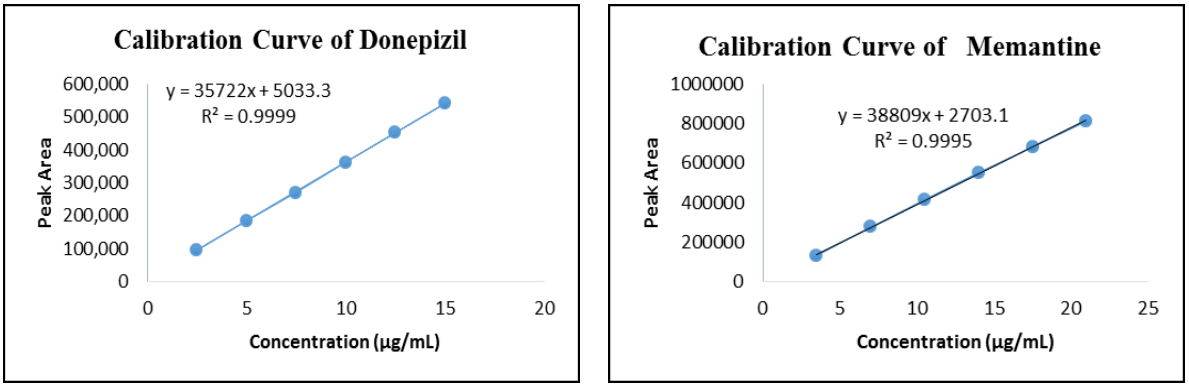


Fig. 4: Calibration Curves Showing Linearity of Memantine and Donepezil by RP-UPLC.

Accuracy

The accuracy of the developed RP-UPLC method was evaluated by % recovery studies at three spiking levels: 50%, 100%, and 150%. The mean % recoveries of Memantine and

Donepezil were within 100 ± 2%, demonstrating the method's accuracy in accordance with ICH Q2(R1) guidelines.

Table 8: Accuracy Results of Memantine and Donepezil.

Drug	% Level	Added (µg/mL)	Recovered (µg/mL)	% Recovery (Mean ± SD)	%RSD	Acceptance Limit
Memantine	50%	7	6.94	98.87 ± 0.10	0.11	98–102%
	100%	14	14.00	99.85 ± 0.55	0.57	98–102%
	150%	21	20.89	99.42 ± 0.38	0.39	98–102%
Donepezil	50%	5	5.01	100.05 ± 0.65	0.65	98–102%
	100%	10	10.03	100.05 ± 0.50	0.50	98–102%
	150%	15	14.91	99.54 ± 0.05	0.07	98–102%

Precision

The method's precision was confirmed by evaluating both intraday and interday variations. The %RSD values for all parameters were below 2%, demonstrating that the developed RP-UPLC method is precise, reproducible, and meets ICH Q2(R1) criteria.

Table 9: Intraday Precision of Memantine and Donepezil.

Drug	Concentration (µg/mL)	RT (min) Mean ± SD	%RSD (RT)	Peak Area Mean ± SD	%RSD (Area)	USP Plate Count Mean ± SD	%RSD (Plate)
Memantine	14	1.174 ± 0.006	0.51	544,193 ± 4,487	0.82	3,062 ± 22	0.72
Donepezil	10	1.668 ± 0.008	0.48	364,125 ± 864	0.24	3,888 ± 23	0.59

Table 10: Interday Precision of Memantine and Donepezil.

Drug	Conc. (µg/mL)	Retention Time (min)	Peak Area	Theoretical Plate Count	USP Tailing Factor	%RSD (Peak Area)
Memantine	14	1.174 ± 0.009	547,354 ± 5,673	3,196 ± 76	1.56 ± 0.09	1.03
Donepezil	10	1.667 ± 0.009	365,508 ± 2,053	3,986 ± 115	1.50 ± 0.07	0.56

Robustness

Minor variations in mobile phase composition, temperature, and flow rate did not significantly affect retention time, peak area, plate count, or tailing factor for either Memantine or Donepezil. All %RSD values remained within acceptable limits (<2%), confirming the robustness of the method. Results are summarized in Table 11.

Table 11: Robustness Evaluation of the RP-UPLC Method for Memantine and Donepezil.

Robustness Parameter	Condition	Memantine (Mean Area ± SD)	%RSD	Donepezil (Mean Area ± SD)	%RSD	Criteria
Mobile Phase Ratio	High (71:29 / 73:27)	567,942 ± 1,620	0.29	368,942 ± 4,520	1.22	%RSD ≤ 2
	Low (69:31 / 67:33)	535,284 ± 2,869	0.54	351,884 ± 1,710	0.49	
Column Temperature	25°C	565,873 ± 3,615	0.69	364,932 ± 3,648	1.00	
	35°C	532,998 ± 3,124	0.48	355,861 ± 2,755	0.77	
Flow Rate	Low (0.2 mL/min)	541,105 ± 5,523	1.02	362,940 ± 3,490	0.96	
	High (0.4 mL/min)	564,852 ± 4,398	0.78	377,862 ± 4,307	1.08	

Specificity

No interference was detected at the retention times of Memantine and Donepezil. Standard and sample peaks were well resolved, while the blank showed no peaks at the respective RTs.

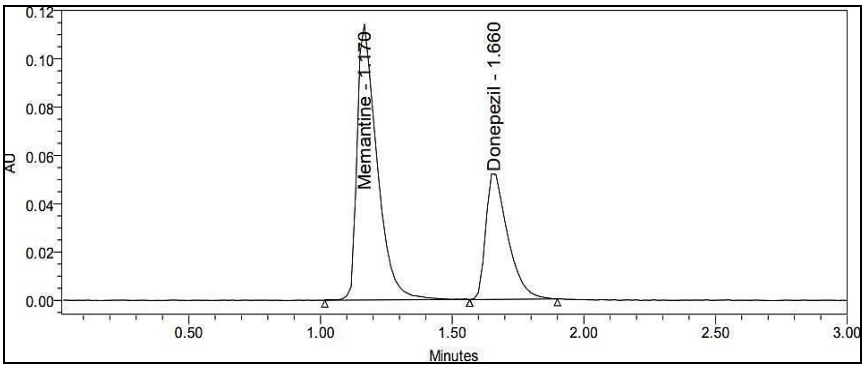


Fig. 5: Chromatogram of Sample Showing the Analyte Peak.

Table 12: Specificity results Memantine and Donepezil.

S. No.	Sample Name	RT (min) – Memantine	RT (min) – Donepezil
1	Standard	1.171	1.659
2	Sample	1.170	1.160
3	Blank	–	–

5.7 Sensitivity

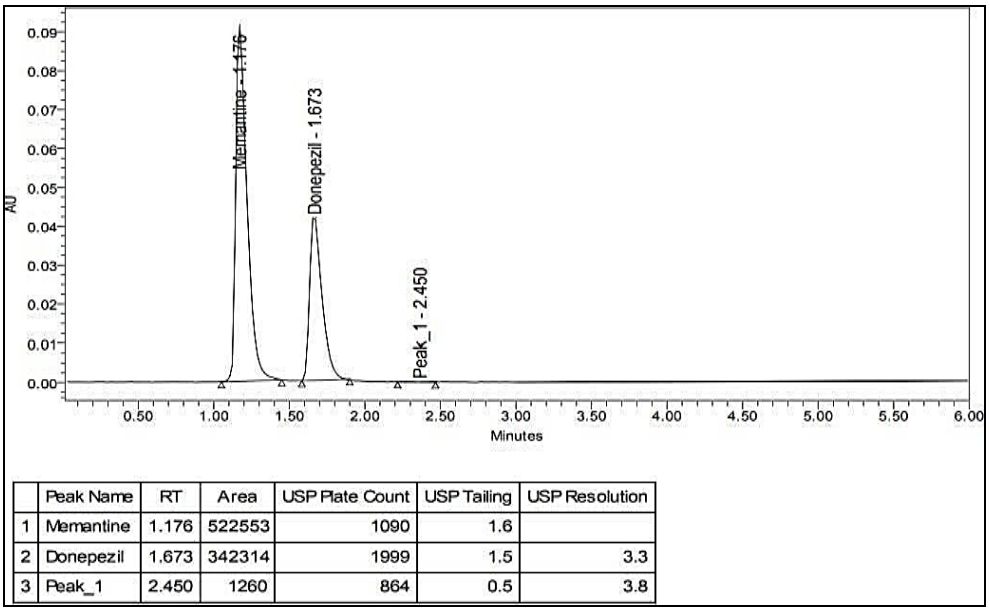
Calculated LOD & LOQ values from the calibration curve.

Table 13: Sensitivity parameters (LOD & LOQ) for Memantine and Donepezil.

Drug	LOD (µg/mL)	LOQ (µg/mL)
Memantine	0.05	0.17
Donepezil	0.01	0.03

Forced Degradation Studies

Forced degradation under various stress conditions showed acceptable degradation levels for both drugs, confirming that the method is stability-indicating. The % degradation results are shown in Table 14.



	Peak Name	RT	Area	USP Plate Count	USP Tailing	USP Resolution
1	Memantine	1.176	522553	1090	1.6	
2	Donepezil	1.673	342314	1999	1.5	3.3
3	Peak_1	2.450	1260	864	0.5	3.8

Fig 6: Acid degradation chromatogram showing formation of degradation peaks and clear separation from the main analyte peaks.

Table 14: Forced Degradation Study of Memantine and Donepezil.

Stress Condition	% Degradation – Memantine	% Degradation – Donepezil
Acidic degradation	4.13	6.22
Alkali degradation	4.07	4.59
Oxidative degradation	6.35	4.99
Thermal degradation	2.49	0.79
Photolytic degradation	2.61	3.46
Neutral degradation	–	0.01

Assay

The assay results for both drugs were within the acceptable range (98–102%), confirming the accuracy and suitability of the developed method. Specifically, Memantine and Donepezil showed assay values of 99.30 ± 0.52% and 99.62 ± 0.61%, respectively.

DISCUSSION

The RP-UPLC method developed in this study for the simultaneous estimation of Memantine and Donepezil demonstrated excellent analytical performance across all validation parameters. The optimized chromatographic conditions yielded sharp, well-resolved peaks, confirming the efficiency and reliability of the method.

Compared to previously reported methods, our approach achieved significantly shorter retention times for both drugs, attributed to the use of the XBridge C18 (100 × 2.1 mm, 1.8 µm) column and a lower flow rate. While earlier studies with larger C18 or C8 columns required longer run times and higher solvent volumes, the present method maintains excellent resolution, linearity, and reproducibility despite the faster analysis.

Linearity was observed for both Memantine and Donepezil within the tested concentration ranges, demonstrating the method's suitability for accurate quantitative determination. Precision and accuracy parameters complied with ICH guidelines, confirming consistent and reproducible results. Specificity studies indicated no interference from blanks or excipients, and stress degradation studies showed clear separation of degradation products from the analytes, confirming the method's stability-indicating capability.

Assay results for both drugs were within acceptable limits, highlighting the method's applicability for routine quality control of pharmaceutical formulations. Overall, the developed RP-UPLC method offers enhanced sensitivity, reduced analysis time, and lower solvent consumption compared with earlier reports, making it a robust and reliable tool for simultaneous estimation of Memantine and Donepezil.

CONCLUSION

The developed RP-UPLC method for the simultaneous estimation of Memantine and Donepezil proved to be simple, precise, accurate, and robust. All validation parameters complied with ICH guidelines, including linearity, system suitability, precision, accuracy, specificity, sensitivity, and robustness. Stress degradation studies confirmed that the method is stability-indicating, with clear separation of analyte peaks from their degradation products. The assay results further demonstrated that the method is suitable for routine quality control analysis. Overall, the method is reliable and effective for the quantitative determination of Memantine and Donepezil in pharmaceutical formulations.

CONFLICT OF INTEREST

The authors have no conflicts of interest regarding this investigation**.**

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REFERENCES

1. Alzheimer's Association. 2023 Alzheimer's disease facts and figures. *Alzheimer's Dement*, 2023; 19(4): 1598-1695.
2. Birks JS, Harvey RJ. Donepezil for dementia due to Alzheimer's disease. *Cochrane Database Syst Rev*., 2018; 6: CD001190.
3. Robinson DM, Keating GM. Memantine: a review of its use in Alzheimer's disease. *Drugs*., 2006; 66(11): 1515–1524.
4. Reisberg B, Doody R, Stoffler A, Schmitt F, Ferris S, Möbius HJ; Memantine Study Group. Memantine in moderate-to-severe Alzheimer's disease. *N Engl J Med*., 2003; 348(14): 1333–1341.
5. Li DD, Zhang YH, Zhang W, Zhao P. Meta-analysis of randomized controlled trials on the efficacy and safety of Donepezil, Galantamine, Rivastigmine, and Memantine in Alzheimer's disease. *Front Neurosci*, 2019; 13: 472.
6. Howard R, McShane R, Lindesay J, Ritchie C, Baldwin A, Barber R, et al. Donepezil and Memantine for moderate-to-severe Alzheimer's disease. *N Engl J Med*., 2012; 366: 893–903.
7. Yaghmaei E, Lu H, Ehwerhemuepha L, et al. Combined use of Donepezil and Memantine increases the probability of five-year survival of Alzheimer's disease patients. *Commun Med*., 2024; 4: 99.
8. Tariot PN, Farlow MR, Grossberg GT, Graham SM, McDonald S, Gergel I; Memantine Study Group. Memantine treatment in patients with moderate to severe Alzheimer's disease already receiving Donepezil. *JAMA*., 2004; 291(3): 317–324.
9. Ahuja S, Scypinski S. *Handbook of Modern Pharmaceutical Analysis*. 2nd ed. Academic Press, 2010.
10. Willard HH, Merritt LL, Dean JA, Settle FA. *Instrumental Methods of Analysis*. 7th ed.

CBS Publishers, 1986.

11. Snyder LR, Kirkland JJ, Dolan JW. *Introduction to Modern Liquid Chromatography*. 3rd ed. Wiley, 2010.
12. Swartz ME, Krull IS. *Analytical Method Development and Validation*. CRC Press, 2012.
13. Gumułka P. UPLC Technique in Pharmacy—An Important Tool of the Modern Analytical Chemistry. *Processes*, 2022; 10(12): 2498.
14. Ford, N., Lee, J., Andrieux-Meyer, I., & Calmy, A. Safety, efficacy, and pharmacokinetics of rilpivirine: systematic review with an emphasis on resource- limited settings. *HIV/AIDS (Auckland, NZ)*, 2011; *3:* 35.
15. Gaucher, G. M. An introduction to chromatography. *Journal of Chemical Education*, 1969; *46*(11): 729.
16. Geetha, G., Raju, K. N. G., Kumar, B. V., & Raja, M. G. Analytical method validation: an updated. *Review. International Journal of Pharmacy and Biological Sciences*, 2012; 64-71.
17. Swartz ME. UPLC: An Introduction and Review. *J Liq Chromatogr Relat Technol*, 2005; 28(7–8): 1253–1263.
18. Ponnekanti K, Godela R, Yagnambhatla R. Concurrent quantification of Memantine and Donepezil via RP-UPLC with stability indicating feature: Method development and validation. *Res J Pharm Technol*, 2024; 17(6): 2907–2914.
19. Folch, J., Busquets, O., Ettcheto, M., Sánchez-López, E., Castro-Torres, R. D., Verdaguer, E. & Camins, A. Memantine for the treatment of dementia: a review on its current and future applications. *Journal of Alzheimer's Disease*, 2018; *62*(3): 1223-1240.
20. Ford, N., Lee, J., Andrieux-Meyer, I., & Calmy, A. Safety, efficacy, and pharmacokinetics of rilpivirine: systematic review with an emphasis on resource- limited settings. *HIV/AIDS (Auckland, NZ)*, 2011; *3:* 35.
21. Gaucher, G. M. An introduction to chromatography. *Journal of Chemical Education*, 1969; *46*(11): 729.
22. Geetha, G., Raju, K. N. G., Kumar, B. V., & Raja, M. G. Analytical method validation: an updated. *Review. International Journal of Pharmacy and Biological Sciences*, 2012; 64-71.
23. Ghosh, S., Bomma, S., Prasanna, V. L., Vidyadhar, S., Banji, D., & Roy, S. Method development and validation of Rilpivirine in bulk and tablet doses form by RP-HPLC method. *Research Journal of Pharmacy and Technology*, 2013; *6*(3): IV.
24. Gita C and Chanda R. Principle, Instrumentation, and Applications of UPLC: a

noveltechnique of liquid chromatography. Open Chemistry Journal, 2016; 3: 1-16.

25. Hotha, K. K., Reddy, S. P. K., Raju, V. K., & Ravindranath, L. K. Forced degradation studies: practical approach - Overview of regulatory guidance and literature for the drug products and drug substances. *International Research Journal of Pharmacy*, 2013; *4*(5): 78–85.
26. ICH. *Quality guidelines Q1A(R2)*, Stability Testing of new drug substances and products.
27. ICH. *Quality guidelines Q1B (R*2), Photo stability testing of new drug substances and products.
28. ICH. *Quality Guidelines Q2(R1)*, Validation of analytical procedures: text and methodology.
29. Izabela, K., Katarzyna, M., Bozena, B., Ewa, G., & Stefan, T. Determination of imipenem and cilastatin in medicinal products by micellar electrokinetic chromatography. *Current Analytical Chemistry*, 2017; *13*(2): 158-166.
30. Jain, N., Joshi, A., Vyas, N., Malviya, S., & Kharia, A. Development and validation of RP-HPLC method for the estimation of Olanzapine in marketed formulation. *Journal of Drug Delivery and Therapeutics*, 2017; *7*(7): 121-122.
31. Navneet et al., 2011; Folch et al., 2018; Tampi & van Dyck, 2007; Anees et al., 2018.
32. Sutthapitaksakul et al., 2021; Jelic & Darreh Shori, 2010; Cacabelos, 2007; Knowles, 2006.
33. Sujana, K.; Gowri Sankar, D.; Abbulu, K. Simultaneous estimation of Donepezil and Memantine by reverse phase HPLC in bulk and pharmaceutical dosage form. Research Journal of Pharmacy and Technology, 2012; 5(7): 958-961.
34. Syeda Noorain Amena; S. H. Rizwan. Stability-indicating analytical method development and validation of Memantine HCl and Donepezil HCl using RP-HPLC. International Journal of Pharmacy and Pharmaceutical Sciences, 2015; 7(11): 204-210.
35. Rajgor, V. M., Parmar, P. T., Patel, C. N., & Patel, A. S. Analytical method development and validation for the simultaneous estimation of memantine HCL and donepezil HCL in bulk and pharmaceutical dosage form. International Journal of Pharmaceutical Research and Bio-Science, 2014; 3(3): 188-197.
36. Ravikumar, R.; Ganesh, M.; Jang, H. Validated stability-indicating simultaneous estimation of Memantine and Donepezil in pharmaceutical formulation by RP-HPLC-DAD. Pharm Lett., 2016; 8(15): 79-87.
37. ICH Expert Working Group. ICH Q2(R1), Validation of Analytical Procedures: Text and Methodology, 2005. (This is a guideline document.)

38. Memantine: efficacy and safety in mild-to-severe Alzheimer's disease. Tampi R.R. & van Dyck C.H. *Neuropsychiatric Disease and Treatment*, 2007; 3(2): 245-258. DOI:10.2147/nedt.2007.3.2.245.
39. Memantine for the Treatment of Dementia: A Review on its Current and Future Applications. Folch J., Busquets O., Ettcheto M. et al. *Journal of Alzheimer's Disease*, 2018; 62(3): 1223-1240. DOI:10.3233/JAD-170672