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A REVIEW ON ANALYTICAL METHOD DEVELOPMENT AND VALIDATION OF PIRACETAM

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ABSTRACT

Piracetam, chemically 2-oxo-1-pyrrolidineacetamide, is a cyclic derivative of gamma-aminobutyric acid (GABA) and is the prototypical member of the "racetam" class of nootropic agents. It is widely used for cognitive impairment, cortical myoclonus, vertigo, dyslexia, and as adjunct therapy in ischemic stroke, and is frequently formulated in fixed-dose combinations with agents such as citicoline and mecobalamin. Because piracetam possesses a weak UV chromophore and no distinct electroactive or ionizable centre, its precise quantitation in bulk drug and pharmaceutical dosage forms has driven the development of a wide range of analytical methods. This review comprehensively summarizes the physicochemical properties, pharmacokinetics, pharmacodynamics, adverse effects, drug interactions, pharmacovigilance data, regulatory status, and marketed formulations of piracetam. Emphasis is placed on reported analytical techniques for its estimation in bulk and dosage forms, including RP-HPLC, HPLC, UPLC, UV– Visible spectrophotometry, and HPTLC, along with validation parameters such as accuracy, precision, linearity, specificity, robustness, LOD, and LOQ evaluated in accordance with ICH Q2(R1) guidelines. Comparative evaluation indicates that RP-HPLC remains the most widely accepted and reliable method for routine quality control and stability-indicating assays, while UV spectrophotometry offers a rapid, economical alternative and emerging HPTLC/green analytical approaches provide sustainable options for combination-product analysis.

KEYWORDS: Piracetam, RP-HPLC, UV Spectrophotometry, HPTLC, ICH Guidelines, Method Validation.

INTRODUCTION

Cognitive and neurological disorders encompass a broad range of conditions affecting memory, learning, coordination, and mental processing, arising from age-related decline, vascular insufficiency, metabolic disturbance, or structural brain injury. Among the pharmacological agents developed to address these conditions, nootropic drugs occupy a distinctive place, being specifically designed to enhance cognitive function, memory, and learning without exerting classical sedative, stimulant, or psychotropic effects.

Piracetam is a cyclic derivative of gamma-aminobutyric acid (GABA) and is recognized as the first and prototypical agent of the "racetam" class of nootropic drugs, from which subsequent analogues such as levetiracetam, oxiracetam, and aniracetam were later derived. Since its introduction in the 1970s by Giurgea and colleagues, piracetam has been used extensively for cognitive impairment, cortical myoclonus, vertigo of central and peripheral origin, dyslexia in children, and as adjunctive therapy following ischemic stroke and coronary artery bypass surgery, and is prescribed in many countries across Europe, Asia, and South America.[1]

Piracetam is believed to act by modulating neuronal membrane fluidity and neurotransmitter systems, including cholinergic, glutamatergic, and noradrenergic pathways, thereby improving synaptic plasticity and neuronal metabolism without acting as a classical stimulant or sedative. Alongside its central effects, piracetam exerts vascular actions, reducing erythrocyte and platelet aggregation and improving microcirculation, which underlies its additional use in circulatory and haematological conditions.[2]

Owing to its broad clinical utility, piracetam is frequently formulated as a single-component product (tablets, syrups, and injectable solutions) as well as in fixed-dose combinations with agents such as citicoline, vinpocetine, cinnarizine, and mecobalamin, particularly in the Indian and other Asian pharmaceutical markets. Typical adult doses range from 800 mg to 4800 mg per day, administered in divided doses, with the exact regimen individualized according to indication and patient response.[3]

With the widespread clinical use of piracetam, both alone and in combination products, the development and validation of reliable, precise, and stability-indicating analytical methods is essential to ensure pharmaceutical quality, safety, and regulatory compliance. Analytical method development plays a critical role in the quantitative estimation of the active pharmaceutical ingredient (API) in bulk drug and finished dosage forms. Techniques such as Reverse Phase High-Performance Liquid Chromatography (RP-HPLC), High-Performance Liquid Chromatography (HPLC), Ultra-Performance Liquid Chromatography (UPLC), UV– Visible spectrophotometry, and High-Performance Thin Layer Chromatography (HPTLC) have been reported for the estimation of piracetam, individually and in combination formulations. Method validation, performed in accordance with International Council for Harmonisation (ICH) Q2(R1) guidelines, evaluates parameters including accuracy, precision, specificity, linearity, robustness, limit of detection (LOD), and limit of quantification (LOQ).[4]

In recent years, emphasis has also been placed on green analytical chemistry approaches, impurity profiling, and quality-by-design (QbD)-based method optimization to minimize environmental impact while maintaining analytical performance. Considering the therapeutic importance of piracetam and the necessity for stringent quality control across its diverse dosage forms, a comprehensive review of analytical method development and validation strategies for piracetam is both timely and scientifically relevant.[5]

Adverse drug reaction

Piracetam is generally well tolerated, and serious adverse reactions are uncommon; however, several effects have been documented in clinical use. Central nervous system effects include drowsiness, nervousness, agitation, insomnia, and hyperkinesia (hyperactivity and muscle spasm), which are typically dose-related and reversible upon dose reduction or discontinuation. Gastrointestinal disturbances such as nausea, vomiting, abdominal pain, and diarrhoea have also been reported, generally mild and self-limiting in nature.[6]

Because piracetam reduces erythrocyte and platelet aggregation and decreases plasma fibrinogen and von Willebrand factor levels, it carries a notable bleeding risk when combined with anticoagulants or antiplatelet agents such as warfarin, aspirin, clopidogrel, or other NSAIDs, and such combinations warrant close monitoring. Allergic skin reactions, including rash, pruritus, and hives, occur rarely, and isolated cases of confusion, hallucination, and worsening of seizure activity in epileptic patients have also been noted. Long-term safety data remain relatively limited, and abrupt discontinuation of high therapeutic doses may occasionally produce a rebound of the symptoms being treated.[7]

Physical and chemical properties

Piracetam

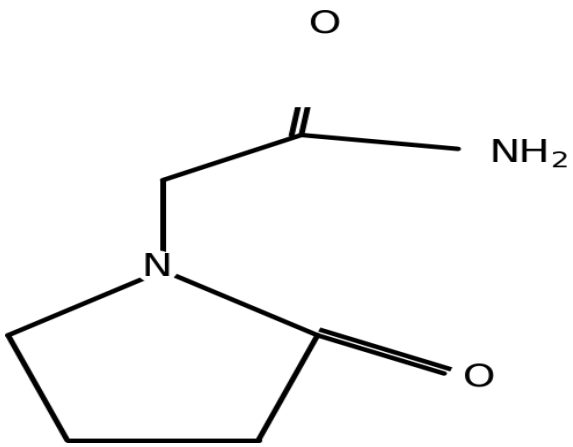

Figure-1: Structure of Piracetam.

The compound, with the IUPAC name 2-(2-oxopyrrolidin-1-yl) acetamide (also referred to as 2-oxo-1-pyrrolidineacetamide), belongs to the pyrrolidinone (racetam) class of nootropic agents. It appears as a white to off-white crystalline powder, is odourless, and has a slightly bitter taste. The molecular formula is $C_6 H_{1\,0} N_2 O_2$, with a molecular weight of approximately 142.16 g/mol. Piracetam is freely soluble in water, slightly soluble in ethanol, and practically insoluble in most non-polar organic solvents such as chloroform and ether, reflecting its predominantly hydrophilic character. The compound has a melting point of approximately 151– 153 ° C, is essentially non-ionizable under physiological pH (weak amide functionality, no distinct acidic or basic pKa in the physiological range), and exhibits a low log P (approximately − 1.2 to − 0.8), consistent with its high aqueous solubility and negligible plasma protein binding. It is chemically stable under normal storage conditions, non-hygroscopic, and relatively resistant to hydrolytic and oxidative degradation, although it may be sensitive to prolonged exposure to strong light, heat, and extremes of pH. Finished pharmaceutical products (tablets, syrups) are typically recommended to be stored at room temperature, generally below 25– 30 ° C, in a cool, dry place protected from moisture and direct light.[8,9]

Drug approval details

Piracetam was first synthesized in 1964 by Corneliu E. Giurgea and colleagues at UCB Pharma in Belgium, who subsequently coined the term "nootropic" to describe its unique cognition-enhancing profile distinct from classical psychostimulants. The drug was introduced into clinical use in Europe in the early 1970s under the brand name Nootropil and has since been approved and marketed as a prescription medicine in numerous countries across Europe, Asia (including India, China, and Southeast Asia), and South America for indications such as cortical myoclonus, cognitive impairment, vertigo, and dyslexia.[10]

In the United States, piracetam has not been approved by the Food and Drug Administration (FDA) as a drug for any medical indication; it is classified as a new unapproved drug and cannot legally be marketed as a treatment for any disease, although it is not a federally scheduled controlled substance and is sold in some jurisdictions as a dietary ingredient. The FDA has issued warning letters to companies marketing piracetam-containing products as dietary supplements, stating that such products do not meet the regulatory definition of a lawful dietary ingredient. In the United Kingdom, piracetam has regulatory approval for use in cortical myoclonus.[11]

In India, piracetam is approved by the Central Drugs Standard Control Organization (CDSCO) and the Drug Controller General of India (DCGI) and is widely marketed as a prescription medicine, both as a single-component product and in fixed-dose combinations with citicoline, vinpocetine, and other neuro-active agents, reflecting its long-standing and extensive clinical use in the Indian pharmaceutical market.[12]

Table-1: pharmaceutical manufacturing companies associated brand information:[13,14]

No.	Brand	Strength	Dosage form	Manufactured by/ Marketed by	Pack size	MRP (₹)
1	Piracetam 400	400 mg	Tablet	IPCA Laboratories / Innova (IPCA)	10's	35.00
2	Piracetam 800	800 mg	Tablet	IPCA Laboratories / Innova (IPCA)	10's	70.00
3	Piracetam 1200	1200 mg	Tablet	IPCA Laboratories / Innova (IPCA)	10's	95.00
4	Cerecetam 400	400 mg	Tablet	Intas Pharmaceuticals Ltd.	10's	80.39
5	Cerecetam 800	800 mg	Tablet	Intas Pharmaceuticals Ltd.	10's	207.50
6	Cerecetam 1200	1200 mg	Tablet	Intas Pharmaceuticals Ltd.	10's	288.75
7	Normabrain 400	400 mg	Capsule	Torrent Pharmaceuticals Ltd.	10’s	32.35
8	Normabrain 800	800 mg	Tablet	Torrent Pharmaceuticals Ltd.	10's	242.62
9	Neurocetam 400	400 mg	Capsule	Micro Labs Ltd.	10's	50.00
10	Neurocetam 800	800 mg	Tablet	Micro Labs Ltd.	10's	632.81
11	Neurocetam 1200	1200 mg	Tablet	Micro Labs Ltd.	10's	221.86
12	Nootropil 400	400 mg	Tablet	Dr. Reddy's Laboratories Ltd.	10's	154.31
13	Nootropil 800	800 mg	Tablet	Dr. Reddy's Laboratories Ltd.	30's	1,084.22
14	Nootropil 1200	1200 mg	Tablet	Dr. Reddy's Laboratories Ltd.	10's	381.56
15	Cetam 400	400 mg	Tablet	Taurus Laboratories Pvt. Ltd.	10's	29.00
16	Cetam 800	800 mg	Tablet	Taurus Laboratories Pvt. Ltd.	10's	85.00
17	Nupic 400	400 mg	Tablet	LA Pharmaceuticals	10's	30.00
18	Nupic 800	800 mg	Tablet	LA Pharmaceuticals	10's	60.00
19	Piracet 400	400 mg	Tablet	D.D. Pharmaceuticals Pvt. Ltd.	10's	69.38
20	Piracet 800	800 mg	Tablet	D.D. Pharmaceuticals Pvt. Ltd.	10's	107.81
21	Pircetam 400	400 mg	Tablet	Knoll Healthcare Pvt. Ltd.	10's	80.00
22	Pircetam 800	800 mg	Tablet	Knoll Healthcare Pvt. Ltd.	10's	158.50
23	Pircetam 1200	1200 mg	Tablet	Knoll Healthcare Pvt. Ltd.	10's	200.00
24	Piratem 800	800 mg	Tablet	Gokul Pharma	10's	95.00
25	PTAM 800	800 mg	Tablet	Suraksha Strategic Solutions Pvt.Ltd.	10's	168.25
26	Tritam 400	400 mg	Capsule	Tripada Healthcare Pvt. Ltd.	10's	97.24

27	Tritam 800	800 mg	Tablet/capsule	Tripada Healthcare Pvt. Ltd.	10's	175.31
28	Pirahenz 800	800 mg	Tablet	La Renon Healthcare Pvt. Ltd.	10's	186.56
29	Apira 800	800 mg	Tablet	Abibba Pharmaa Pvt. Ltd.	10's	66.00
30	Piramax 400	400 mg	Tablet	Biomax Lab	10's	40.00
31	Ultacetam 400	400 mg	Tablet	Ultra Chiron	10's	43.00
32	Hicetam 400	400 mg	Tablet	Redson Lab	10's	43.00
33	Ceact 400	400 mg	Tablet	Crescent Therapeutics Ltd.	10's	53.00
34	Ceact 800	800 mg	Tablet	Crescent Therapeutics Ltd.	10's	102.50
35	Flocetam 800	800 mg	Tablet	Macsur Pharmaa (India) Pvt. Ltd.	10's	154.69
36	Neucet 800	800 mg	Tablet	Royal Labs	10's	70.00
37	TAM 800	800 mg	Tablet	Octane Biotech	10's	78.00
38	Normenta 400	400 mg	Capsule	Makers Laboratories	10's	42.00
39	Normenta 800	800 mg	Tablet	Makers Laboratories	10's	80.90
40	Ubittor 800	800 mg	Tablet	Ubit Pharma	10's	85.00
41	Zetam 800	800 mg	Tablet	Allenge India	10's	85.00
42	Neetam 800	800 mg	Tablet	Mankind Pharma / Magnet Labs	10's	89.00
43	Nutam 800	800 mg	Film-coated tablet	Molekule India Pvt. Ltd.	10's	92.00
44	Nutam 1200	1200 mg	Film-coated tablet	Molekule India Pvt. Ltd.	10's	105.00
45	Pirac 800	800 mg	Tablet	Orchid	10's	98.00
46	Braintam 400	400 mg	Tablet	Total Health Care	10's	44.00
47	Biocetam 800	800 mg	Tablet	Paradigm Health Care	10's	81.00
48	Cerabol 800	800 mg	Tablet	BIPL	10's	83.30
49	PITAM 1200	1200 mg	Tablet	Chemo Biological	10's	125.00
50	Piramet 400	400 mg	Tablet	IPCA Laboratories	10's	35.00
51.	Cognitam-400	400 mg	Tablet	Linux laboratories		90.35

Analytical method development and validation of piracetam[15]

Several analytical methods have been reported for the quantitative estimation of piracetam in bulk drug and pharmaceutical dosage forms. The commonly used techniques include UV-visible spectrophotometry, RP-HPLC, HPTLC, UPLC, FTIR, and LC-MS/MS. UV spectrophotometric methods are simple, rapid, economical, and suitable for routine estimation of piracetam; however, their specificity is limited because piracetam shows absorption mainly in the low-UV region and interference may occur from excipients or other drugs.

RP-HPLC is one of the most widely reported methods for piracetam because of its good specificity, accuracy, precision, and reproducibility. C18 or C8 columns with aqueous buffers and organic solvents such as methanol or acetonitrile are commonly used, with UV detection generally performed in the low-UV region. RP-HPLC has been successfully applied to the simultaneous estimation of piracetam with drugs such as levetiracetam, citicoline, vincamine, and cinnarizine in fixed-dose formulations. Stability-indicating RP-HPLC methods have also been developed to separate piracetam from its degradation products.

HPTLC and TLC methods provide relatively simple and economical alternatives to HPLC and have been used for assay determination and related-substance profiling of piracetam. UPLC methods offer improved chromatographic efficiency, shorter analysis time, lower solvent consumption, and better sensitivity than conventional HPLC, making them useful for stability and impurity studies. FTIR spectroscopy has been investigated for identification and quantitative determination of selected piracetam-related impurities, while LC-MS/MS methods are mainly used for sensitive determination of piracetam in biological samples during pharmacokinetic and bioequivalence studies.

Overall, RP-HPLC and UPLC are considered particularly suitable for specific and stability-indicating analysis of piracetam, whereas UV spectrophotometry and HPTLC are useful for simpler routine quality-control applications. The selection of the analytical method depends on the formulation, required sensitivity, presence of other active ingredients, and whether the objective is assay determination, impurity profiling, or stability evaluation.

Table-2: Different Analytical Method Development and Validation of Piracetam.

S. No.	Analytical method	Title of article	Detailed analytical parameters	Year / Month	Ref.
1	UV–Visible spectrophotometry – first derivative	Analytical Method Development and Validation for Piracetam as Bulk and in Pharmaceutical Formulation	• Sample: Bulk drug + pharmaceutical formulation • Solvent: Methanol • Technique: First-order derivative UV spectroscopy • Detection wavelength: 214 nm • Linearity: 10–80 µg/mL • Accuracy: Mean recovery 99.35% • Validation: Specificity, linearity, precision, accuracy, ruggedness • Application: Routine assay of piracetam	2010 / Jan–Mar	[16]
2	RP-HPLC	HPLC Determination of Piracetam in Tablets; Validation of the Method	• Sample: Piracetam film-coated tablets • Column: LiChrospher 100 RP-18, 5 µm • Mobile phase: Methanol: water (5:95, v/v) • Flow rate: 1.2 mL/min • Injection volume: 20 µL • Detection: 215 nm • Linearity: 100–1000 µg/mL in the original method • Forced degradation: HCl, NaOH and H_2O_2 • Validation: Selectivity, accuracy, precision, robustness, DL and QL • Application: Routine tablet assay	2005 / May	[17]
3	RP-HPLC–UV impurity profiling	Simultaneous Determination of Piracetam and Its Four Impurities by RP-HPLC with UV Detection	• Sample: Piracetam bulk drug/API • Column: C18 Nucleosil • Mobile phase: 0.02% triethylamine: acetonitrile (85:15, v/v) • pH: 6.5, adjusted with orthophosphoric acid • Detection: 205–206 nm • Linearity: 0.05–10 µg/mL • Application: Separation/quantification of piracetam and four related impurities • Type: Impurity profiling/QC	2010	[18]
4	UPLC	Establishment of Inherent Stability on Piracetam by UPLC/HPLC and Development of a Validated Stability-Indicating Method	• Sample: Piracetam drug substance/formulation • Column: Acquity UPLC BEH C18 • Particle size: 1.7 µm • Mobile phase: Acetonitrile: water (25:75, v/v) • Detection: UV/PDA • Linearity: 10–50 µg/mL • Forced degradation: Acidic, alkaline, oxidative, thermal and photolytic conditions • Application: Stability-indicating assay	2013 / online 2012	[19]
5	TLC–densitometry	Determination of Piracetam and Its Impurities by TLC	• Sample: Piracetam + related impurities • Stationary phase: TLC silica plate • Mobile phase: Pentyl acetate: ethyl acetate: ethanol: glacial acetic acid (10:10:9:1) • Detection: Gibb's reagent–ammonia vapor • Densitometric measurement: Sample 210 nm; reference 230 nm • Application: Separation/detection of related impurities • Impurities studied: 2-oxopyrrolidine, 2-oxo-1-	2000 / Sep	[20]

			pyrrolidine acetic acid, methyl acetate and ethyl acetate derivatives		
6	HPTLC	Estimation of Piracetam in Bulk and Formulation Using High Performance Thin-Layer Chromatography	• Sample: Pure piracetam + tablets • Plate: Silica gel 60F254 • Plate size: 10 × 10 cm • Mobile phase: Chloroform: methanol: glacial acetic acid: triethylamine (16:4:0.2:0.2) • Application: CAMAG Linomat-5 • Development chamber: Twin-trough chamber • Detection: 254 nm • Linearity: Standard application 1–10 µL • Precision: %RSD 0.31 • Accuracy: %RSD 0.59 • Application: Bulk drug and tablet assay	2023 / Mar	[21]
7	FTIR spectroscopy	Determination of Possible Impurities in Piracetam Using FTIR Spectroscopy	• Sample: Piracetam bulk drug • Technique: FTIR spectroscopy • Application: Identification/estimation of related impurities • Target: Possible process/degradation impurities • Reported range: 0.1–1.3 mg impurity/mg sample in the systematic review • Nature: Qualitative/semi-quantitative impurity assessment • Purpose: Drug identity and impurity/degradation evaluation	2000	[22]
8	Capillary electrophoresis (CE)	Determination of Piracetam in Human Plasma by Capillary Electrophoresis	• Matrix: Human plasma • Capillary: Uncoated silica capillary • Buffer: Borax buffer + α-cyclodextrin • Detection: UV 200 nm • Linearity: 4–24 µg/mL • Detection limit: 1 µg/mL • Inter-assay RSD: <9.3% • Application: Bioavailability/clinical studies	1997 / May	[23]
9	GC–NPD	New Validated Gas-Chromatographic Method for Piracetam Determination in Plasma	• Matrix: Human and rat plasma • Technique: Gas chromatography • Column: Fused-silica capillary column • Detector: Nitrogen-phosphorus detector (NPD) • Internal standard: Tripelennamine • Linearity: 0.1–100 µg/0.5 mL plasma • LOQ: 0.1 µg/0.5 mL • LOD: 0.01 µg/0.5 mL • Application: Pharmacokinetic/bioequivalence studies	1997	[24]
10	GC	Determination of Piracetam in Serum by Gas Chromatography	• Matrix: Human serum • Technique: Gas chromatography • Application: Quantitative determination of piracetam in serum • Purpose: Pharmacokinetic/clinical analysis	1990 / Apr	[25]
11	HPLC–UV	Determination of Piracetam in Human Plasma and Urine by Liquid Chromatography	• Matrix: Human plasma and urine • Column: Hibar LiChrosorb RP-18 • Mobile phase: Methanol:water (5:95) • Mode: Isocratic • Detection: 206 nm • Extraction: Hexane–2-propanol at pH 9.2 • Linearity: 3–40 mg/L plasma; 100–2000 mg/L urine • LOQ: 3 mg/L plasma; 100 mg/L urine	1995 / Jan	[26]
12	HPLC–UV	New Validated Method for Piracetam HPLC Determination in Human Plasma	• Matrix: Human plasma • Column: RP-18 LiChroSpher 100 • Mobile phase: Aqueous 0.01% $HClO_4$ + acetonitrile + methanol	2007	[27]

			• Mode: Gradient • Detection: 200 nm • Linearity: 5–80 µg/mL • Sample preparation: Perchloric-acid protein precipitation • Application: Pharmacokinetic/bioequivalence analysis		
13	HPLC–UV microanalytical	A High-Performance Liquid-Chromatographic Microanalytical Procedure for the Rapid Estimation of Piracetam in Plasma or Cerebrospinal Fluid	• Matrix: Plasma / CSF • Plasma volume: 25 µL • CSF volume: 10 µL • Column: Spherisorb S5CN • Mobile phase: Acetonitrile: water (98:2) • Internal standard: α-ethyl-2-oxo-1-pyrrolidine acetamide • Detection: 215 nm • Linearity: 4–256 µg/mL • Application: Pharmacokinetic analysis	1996 / May	[28]
14	HPLC–UV	Liquid-Chromatographic Quantification of Piracetam	• Matrix: Rabbit serum and aqueous humor • Column: Bondapak C18 • Mobile phase: Methanol + 0.1 M KH_2PO_4 • pH: 4.8 • Detection: 208 nm • Linearity: 5–15 nmol • Application: Quantitative determination in biological samples	1983 / Apr	[29]
15	MEKC	Rapid Determination of Piracetam in Human Plasma and Cerebrospinal Fluid by Micellar Electrokinetic Chromatography with Sample Direct Injection	• Matrix: Human plasma and CSF • Technique: Micellar electrokinetic chromatography • Background electrolyte: Tris buffer + SDS • Internal standard: Imidazole • Temperature: 25°C • Linearity: 5–500 µg/mL • LOD: 1 µg/mL • Application: Clinical/pharmacokinetic analysis	2005 / Dec	[30]
16	LC–MS/MS	Determination of Piracetam in Rat Plasma by LC–MS/MS and Its Application to Pharmacokinetics	• Matrix: Rat plasma • Column: Zorbax SB-Aq • Mobile phase: Acetonitrile:1% formic acid (10:90) • Internal standard: Oxiracetam • Sample preparation: 5% trichloroacetic acid protein precipitation • Linearity: 0.1–20 µg/mL • Technique: LC–MS/MS • Application: Pharmacokinetic studies	2010 / Oct	[31]

Table-3: Comprehensive analytical-method for Piracetam in combination with other drugs.

S. No.	Analytical method	Drug combination	Title of article	Detailed analytical parameters	Year / Month	Ref.
1	UV–Visible spectrophotometry – simultaneous equation	Cinnarizine + Piracetam	RP-HPLC and UV Methods for Simultaneous Estimation of Fixed Dose Combinations of Cinnarizine and Piracetam: Simultaneous Equation, Experimental Design and Statistical Correlation	• Sample: Combined pharmaceutical formulation • Solvent: Methanol • Technique: Simultaneous-equation method • λmax: 250 nm for cinnarizine; 229 nm for piracetam • Application: Simultaneous quantitative estimation • Method development: Design of experiments (DoE) • Validation: Accuracy, precision, linearity and other ICH parameters	2024 / Aug	[32]

2	UV spectrophotometry – derivative/ratio spectra	Cinnarizine + Piracetam	Spectrophotometric and LC determination of two binary mixtures containing antihistamins	• Sample: Synthetic mixtures and commercial tablets • Technique: Partial least-squares (PLS-1), principal-component regression (PCR) and second-derivative ratio spectra (2DD) • HPLC comparison also performed • Application: Resolution of overlapping spectra and simultaneous determination	2004 / Sep	[33]
3	UV spectrophotometry – ratio spectra first derivative	Piracetam + Vincamine	Simultaneous Determination of Piracetam and Vincamine by Spectrophotometric and High-Performance Liquid Chromatographic Methods	• Technique: Ratio-spectra first-derivative spectrophotometry (DD_1) • Detection wavelengths: 209 nm for piracetam; 293 nm for vincamine • Piracetam linearity: approximately 10–45 µg/mL • Vincamine linearity: approximately 2–14 µg/mL • Mean recovery: Piracetam 99.22%; Vincamine 99.67% • Application: Simultaneous estimation	2008 / Mar	[34]
4	UV spectrophotometry – absorption correction / Q-absorbance	Citicoline + Piracetam	UV-Spectrophotometric Methods for Determination of Citicoline Sodium and Piracetam in Pharmaceutical Formulation	• Sample: Combined dosage form • Methods: Absorption-correction method and Q-absorbance method • Absorption correction: Citicoline measured at 266 nm; piracetam measured at approximately 226.5 nm after correction • Q-absorbance method: wavelengths around piracetam λmax and iso absorptive point • Reported linearity: approximately 10–50 µg/mL citicoline and 100–500 µg/mL piracetam • Validation: Accuracy, precision, linearity and ruggedness	2011	[35]
5	RP-HPLC–UV	Citicoline + Piracetam	Optimization and Validation for Simultaneous Estimation of Citicoline and Piracetam in Bulk and Tablet Formulations Using RP-HPLC Method: Analytical Quality by Design Approach	• Column: C18 • Mobile phase: Acetonitrile: 10 mM disodium hydrogen phosphate buffer 10:90 v/v • Flow rate: 1.0 mL/min • Detection: 205 nm • Run time: 16 min • Rt: Citicoline 3.79 min; Piracetam 13.08 min • Linearity: Citicoline 4–40 µg/mL; Piracetam 5–50 µg/mL • Validation: Accuracy, precision, linearity, specificity and sensitivity • Application: Bulk drug and tablets	2017 / Jul	[36]
6	RP-HPLC–UV	Citicoline + Piracetam	Simultaneous Determination of Piracetam and Citicoline in Combination Drug Products by RP-HPLC Method	• Sample: Synthetic combination mixtures • Mobile phase: Buffer: acetonitrile 60:40 v/v • Detection: 265 nm • Run time: 5 min • Rt: Piracetam 3.158 min; Citicoline 5.196 min • Validation: Linearity, accuracy, precision, LOD, LOQ and system suitability • Application: Routine determination in combination products	2021 / Aug	[37]
7	RP-HPLC–UV	Citicoline + Piracetam	RP-HPLC Method Development for the Simultaneous Estimation of Piracetam and Citicoline in Pharmaceutical Dosage Form	• Column: Phenomenex Luna C18, 250 × 4.6 mm, 5 µm • Mobile phase: Ammonium acetate buffer pH 5.0 : acetonitrile 75:25 • Flow rate: 1.3 mL/min • Detection: 230 nm • Rt: Piracetam 3.020 min; Citicoline 3.796 min • Linearity: approximately 20–75 µg/mL • Accuracy: Piracetam 98–102%; Citicoline 97–101% • Application: Pharmaceutical dosage form	2024	[38]
8	HPLC–UV/PDA –	Cinnarizine + Piracetam	Stability Indicating and Simultaneous	• Column: Hypersil BDS C8, 250 × 4.6 mm, 5 µm • Mobile phase A: Dipotassium hydrogen phosphate +	2013 / Sep	[39]

	stability indicating		Determination of Cinnarizine and Piracetam from Capsule Dosage Form by Reversed Phase High Performance Liquid Chromatography	triethylamine/acetonitrile • Mobile phase B: Orthophosphoric acid in acetonitrile • Mode: Gradient elution • Flow rate: 0.6 mL/min • Detection: 205 nm, DAD • Rt: Piracetam ≈ 11 min; Cinnarizine ≈ 51 min • Stress: Acid, alkali, peroxide, UV and heat • Application: Stability-indicating assay		
9	RP-HPLC / RP-LC	Cinnarizine + Piracetam	Development and Validation of RP-LC Method for the Determination of Cinnarizine/ Piracetam and Cinnarizine/ Heptaminol Acefyllinate in Presence of Cinnarizine Reported Degradation Products	• Column: Hypersil BDS C18, 200 × 4.6 mm, 5 µm • Detector: DAD/UV • Sample: Pharmaceutical formulations and degradation products • Combinations studied: Cinnarizine/Piracetam and Cinnarizine/Heptaminol acefyllinate • Application: Simultaneous assay and degradation-product separation • Validation: Specificity, accuracy, precision and robustness	2013	[40]
10	HPLC–UV	Cinnarizine + Piracetam	Spectrophotometric and LC Determination of Two Binary Mixtures Containing Antihistamins	• Column: RP18 • Mobile phase: Acetonitrile: 0.05 M KH_2PO_4: triethylamine 50:50:0.2 v/v/v • pH: 3.0 • Detection: 227 nm • Sample: Synthetic mixtures and commercial tablets • Application: Simultaneous quantitative determination	2004 / Sep	[41]
11	HPTLC / TLC–densitometry	Citicoline + Piracetam	Development and Validation of Stability Indicating Chromatographic Methods for Simultaneous Determination of Citicoline and Piracetam	• Stationary phase: Silica gel plate • Mobile phase: Methanol: chloroform: ammonium chloride buffer 9:1:2 v/v/v • Detection: 230 nm • Sample: Combined dosage form • Stress studies: Acidic, alkaline, oxidative, thermal and photolytic conditions • Application: Simultaneous determination in presence of degradation products • Validation: Stability indicating, specificity, accuracy and precision	2020 / Jun	[42]
12	UPLC–UV/PDA	Citicoline + Piracetam	Development and Validation of Stability Indicating Chromatographic Methods for Simultaneous Determination of Citicoline and Piracetam	• Mobile phase: Water containing 0.1% triethylamine: ethanol 92:8 v/v • Flow rate: 1.0 mL/min • Detection: 230 nm • Sample: Combination formulation • Stress conditions: Acid, base, oxidation, heat and photolysis • Application: Stability-indicating simultaneous assay • Additional feature: Greenness assessment showed advantages compared with conventional HPLC methods	2020 / Jun	[43]
13	DRS-FTIR + chemometrics	Cinnarizine + Piracetam	Environmentally Sustainable DRS-FTIR Probe Assisted by Chemometric Tools for Quality Control Analysis of Cinnarizine and Piracetam Having Diverged Concentration Ranges	• Technique: Diffuse-reflectance FTIR (DRS-FTIR) • No prior chromatographic separation • Sample: Pharmaceutical dosage form • Ratio: Cinnarizine/Piracetam approximately 1:16 • Data processing: Chemometric calibration • Application: Simultaneous assay and drug dissolution/QC • Advantage: Green, rapid, non-destructive analysis	2023 / Dec	[44]

14	LC–MS/MS	Piracetam + Vincamine	Development and Validation of a Novel LC-MS/MS Method for Sensitive Simultaneous Quantification of Piracetam and Vincamine in Human Plasma	• Matrix: Human plasma • Technique: LC–MS/MS • Purpose: Pharmacokinetic studies, bioequivalence and therapeutic monitoring • Combination ratio: Approximately 1:20 • LLOQ: Piracetam 150 ng/mL; Vincamine 1.0 ng/mL • Application: Simultaneous bioanalytical quantification	2026 / May	[45]
15	HPLC–MS/MS	Piracetam + L-carnitine	Pharmacokinetic Interaction between Piracetam and L-Carnitine in Human Plasma	• Matrix: Human plasma • Technique: HPLC–MS/MS • Internal standard: Piracetam-d8 • Sample preparation: One-step protein precipitation using acetonitrile • Application: Pharmacokinetic interaction study • Purpose: Simultaneous/interaction assessment of piracetam and L-carnitine	2020	[46]
16	UPLC–MS/MS	Piracetam + metabolite M1	Chromatographic Separation of Piracetam and Its Metabolite in a Mixture of Microsomal Preparations, Followed by an MS/MS Analysis	• Matrix: Human liver microsomal preparations and rat plasma • Column: BEH C18 • Mobile phase: Acetonitrile + 10 mM ammonium acetate, pH 5 • Technique: Fast isocratic UPLC–MS/MS • Ionisation: Electrospray ionisation • Application: Simultaneous determination of piracetam and its phase-I metabolite • Purpose: Metabolism and pharmacokinetic investigation	2013	[47]

Pharmacological action of piracetam

Piracetam is a nootropic drug and a cyclic derivative of GABA that is mainly used to improve cognitive function. Although its exact mechanism of action is not completely understood, piracetam is thought to influence neuronal membrane fluidity, neurotransmission, and synaptic function. It can enhance the function of neuronal cell membranes and improve communication between neurons, thereby potentially supporting learning, memory, attention, and other cognitive processes. Piracetam also appears to have effects on microcirculation and red blood cell deformability. It can increase erythrocyte flexibility and reduce platelet aggregation, which may improve blood flow through the microcirculation. It does not act primarily as a sedative, stimulant, or conventional GABAergic drug despite being structurally related to GABA. Pharmacologically, the major proposed actions of piracetam include modulation of neuronal membrane function, enhancement of neurotransmission, improvement of synaptic plasticity, neuroprotective effects, and improvement of cerebral microcirculation. These properties form the basis for its investigation and use in conditions associated with cognitive impairment and certain neurological disorders. The precise molecular mechanism responsible for its clinical effects, however, remains incompletely established.[48]

Pharmacokinetic (ADME) properties

Piracetam is rapidly and almost completely absorbed after oral administration, exhibiting an oral bioavailability close to 100%, with peak plasma concentrations (Tmax) typically reached within 30 minutes to 1.3 hours; food intake does not significantly alter the extent of absorption but may reduce Cmax by approximately 17% and delay Tmax slightly. The drug is negligibly bound to plasma proteins (< 10– 20%) and is widely distributed to most body tissues, crossing both the blood– brain barrier and the placental barrier, with preferential concentration in the grey matter of the cerebrum and cerebellum; it does not accumulate appreciably in adipose tissue. Piracetam is not appreciably metabolized in the

human body, and it is excreted essentially unchanged in the urine via glomerular filtration, accounting for approximately 90– 100% of the administered dose. The plasma elimination half-life in healthy adults is approximately 4– 6 hours (with a somewhat longer half-life of around 8 hours in cerebrospinal fluid), and this half-life is prolonged in elderly patients and in those with renal impairment, necessitating dose adjustment based on creatinine clearance in such populations. Its pharmacokinetics are linear over a wide dose range (0.8– 12 g), and because piracetam does not undergo hepatic metabolism or significantly inhibit major cytochrome P450 isoforms, its potential for metabolic drug– drug interactions is low.[49,50]

Pharmacodynamic properties

The precise molecular mechanism of piracetam remains incompletely understood, but it is believed to act primarily by modulating neuronal membrane fluidity and enhancing neurotransmission across cholinergic, glutamatergic (AMPA-receptor-mediated), and noradrenergic systems, thereby facilitating synaptic plasticity, information transfer between the cerebral hemispheres, and neuronal energymetabolism (via effects on mitochondrial function and ATP/ADP ratios) without producing generalized CNS stimulation or sedation. Additionally, piracetam exerts vascular and hemorheological effects, including reduced erythrocyte and platelet aggregation, decreased plasma fibrinogen and von Willebrand factor concentrations, increased red-cell deformability, and enhanced microcirculatory flow, which contribute to its use in vertigo and post-stroke recovery. These combined neuronal and vascular actions underlie its reported benefits in cognitive impairment, cortical myoclonus, dyslexia, and vertigo, although rigorous evidence for efficacy in established dementia remains limited.[51]

Pharmacovigilance of Piracetam

Piracetam has a generally favorable safety profile based on its long history of clinical use and available clinical and post-marketing safety data. The commonly reported adverse effects include nervousness, insomnia, drowsiness, headache, hyperkinesia, nausea, abdominal discomfort, vomiting, and diarrhea. These reactions are generally mild and manageable with appropriate clinical monitoring. An important pharmacovigilance consideration is piracetam's effect on platelet aggregation and haemostasis, which warrants caution in patients receiving anticoagulant or antiplatelet medicines and in patients with an increased risk of bleeding. Rare hypersensitivity reactions and hematological abnormalities may also occur. Since piracetam is eliminated predominantly as unchanged drug through the kidneys, renal function should be assessed and the dose adjusted in patients with renal impairment, particularly elderly patients. Overall, continued pharmacovigilance is important for detecting rare or unexpected adverse drug reactions and evaluating the safety of piracetam during long-term use.[52,53,54]

Drug interaction of piracetam

Because piracetam is not appreciably metabolized by hepatic cytochrome P450 enzymes and does not significantly inhibit major CYP isoforms, its potential for classical metabolic drug– drug interactions is low, and it has no known severe or serious pharmacokinetic interactions with other medications. Nonetheless, several clinically relevant pharmacodynamic interactions have been reported. Concomitant use with anticoagulants (e.g., warfarin) or antiplatelet agents (e.g., aspirin, clopidogrel) and other NSAIDs may increase bleeding risk due to the additive antithrombotic/anti-platelet effects of piracetam, necessitating closer monitoring of coagulation status in such patients. Co-administration with other CNS-active agents may occasionally potentiate CNS effects such as nervousness or insomnia. In patients with thyroid disease, isolated adverse reactions have been reported, and caution is advised. Because piracetam is

renally excreted, drugs or conditions that reduce renal clearance can increase piracetam plasma levels and prolong its half-life, requiring dose adjustment. Overall, piracetam is considered to have a comparatively low drug-interaction burden relative to many other CNS-active agents, but the bleeding-risk interaction in particular merits specific clinical attention.[55]

Regulatory details of piracetam

Piracetam is a centrally acting nootropic medicine whose regulatory status differs between countries. In India, piracetam is regulated under the Drugs and Cosmetics Act, 1940 and Drugs Rules, 1945. It is included in Schedule H, which identifies prescription drugs and subjects their sale and distribution to prescription-related requirements. Consequently, pharmaceutical formulations containing piracetam must comply with the applicable requirements for manufacture, licensing, sale, labelling, packaging and quality control under the Indian drug regulatory framework. The current CDSCO Drugs Rules page also provides the latest published version of the Drugs Rules and subsequent amendments, which should be consulted when assessing the regulatory status of a particular piracetam formulation.[56]

In the European Union, piracetam is not simply classified as a single centrally authorised EMA medicine; rather, the European Medicines Agency maintains documentation showing piracetam-containing medicinal products that are nationally authorised in individual EU Member States. The EMA's list includes products such as Nootropyl in different strengths and dosage forms, demonstrating that authorisation and marketing conditions can depend on the individual Member State. Therefore, the regulatory status, approved indications, dosage forms and conditions of supply for piracetam should be verified according to the specific country and product concerned.[57]

CONCLUSION

In conclusion, piracetam remains a therapeutically important and widely used nootropic agent for the management of cognitive impairment, cortical myoclonus, vertigo, and dyslexia, and continues to be formulated both as a single-component product and in fixed-dose combinations with agents such as citicoline and mecobalamin. Its favourable pharmacokinetic profile — near-complete oral bioavailability, minimal metabolism, and predominantly renal elimination — supports flexible, well-tolerated dosing, while its combined neuromodulator and hemorheological actions underlie its broad clinical utility. From an analytical standpoint, the weak intrinsic chromophore of piracetam has driven the development of a diverse toolkit of validated methods — UV spectrophotometry, RP-HPLC, UPLC, and HPTLC — each validated in accordance with ICH Q2(R1) guidelines for specificity, linearity, accuracy, precision, LOD/LOQ, and robustness. RP-HPLC remains the most widely accepted platform for routine quality control and stability-indicating assays, particularly for combination formulations, while UV spectrophotometry offers a rapid and economical alternative, and HPTLC together with emerging green/QbD-optimized approaches provide sustainable options for future method development. Continued pharmacovigilance, particularly regarding bleeding risk in combination with antithrombotic agents and dose adjustment in renal impairment, together with ongoing refinement of stability-indicating analytical methodologies, will further strengthen the safe and effective use of piracetam-containing formulations.

REFERENCES

1. Giurgea C, Salama M. Nootropic drugs. Prog Neuropsychopharmacology, 1977; 1(3-4): 235-247.
2. Gouliaev AH, Senning A. Piracetam and other structurally related nootropics. Brain Res Rev, 1994; 19(2): 180-222.

3. Winblad B. Piracetam: a review of pharmacological properties and clinical uses. CNS Drug Rev, 2005; 11(2): 169-182.
4. International Council for Harmonisation (ICH). ICH Q2(R1): Validation of Analytical Procedures - Text and Methodology. Geneva: ICH; 2005.
5. Sen AK, Sarkar TK, Sen DB. Green analytical chemistry and quality-by-design approaches in pharmaceutical method development: a review. J Pharm Anal Insights, 2023.
6. MedIndia. Piracetam drug information - indications, dosage, sideffects and precautions.
7. Biomedicus. The side effects of Nootropil (piracetam).
8. PubChem. Piracetam compound summary (CID information, physicochemical properties). National Library of Medicine.
9. ChemicalBook. Piracetam – pharmacological effects and pharmacokinetics; physicochemical property data.
10. Gouliaev AH, Senning A. Piracetam and other structurally related nootropics. Brain Res Rev, 1994; 19(2): 180-222.
11. MedicineNet. Piracetam: Alzheimer's & dementia uses, warnings, side effects, dosage.
12. Central Drugs Standard Control Organization. Approved drugs list and regulatory updates.
13. MIMS India. Piracetam: drug information and available brands. Mumbai: MIMS India; 2026.
14. Medicine India. Medicine brands for generic piracetam. India: Medicine India; 2026. And Apollo Pharmacy. Piracetam-containing tablet substitutes and brand comparisons India: Apollo Pharmacy; 2026.
15. Sahu K, Kundu P, Pal A, et al. Establishment of inherent stability on piracetam by UPLC/HPLC and development of a validated stability-indicating method. *Arab J Chem*, 2017; 10: S1118-S1127.
16. Bhowmick AA, Khandelwal KR, Mhaske DV, Khadke S. Analytical method development and validation for piracetam as bulk and in pharmaceutical formulation. *Int J PharmTech Res*, 2010; 2(1): 201-204.
17. Lestari AD, Prasetyo AT, Palupi T, Umayah E, Yuwono M, Indrayanto G. HPLC determination of piracetam in tablets; validation of the method. *J Liq Chromatogr Relat Technol*, 2005; 28(9): 1407-1416.
18. Arayne MS, Sultana N, Siddiqui FA, Mirza AZ, Qureshi F, Zuberi MH. Simultaneous determination of piracetam and its four impurities by RP-HPLC with UV detection. *J Chromatogr Sci*, 2010; 48(7): 589-594.
19. Sahu K, Shaharyar M, Siddiqui AA, Sahu S. Establishment of inherent stability on piracetam by UPLC/HPLC and development of a validated stability-indicating method. *Arab J Chem*, 2017; 10(Suppl 1): S576-S582.
20. Ovalles JF, Tettey JNA, Miller JHMcB, Skellern GG. Determination of piracetam and its impurities by TLC. *J Pharm Biomed Anal*, 2000; 23(4): 757-761.
21. Sam Solomon WD, Priyadharshini R, Hemamalini K, Karnan V, Priyavagini S, Anjana KR. Estimation of piracetam in bulk and formulation using high performance thin-layer chromatography. *Int J Innov Sci Res Technol*, 2023; 8(3): 2052-2056.
22. Karamancheva I, Staneva T. Determination of possible impurities in piracetam using FTIR spectroscopy. *J Pharm Biomed Anal*, 2000; 21(6): 1161-1169.
23. Lamparczyk H, Kowalski P, Rajzer D, Nowakowska J. Determination of piracetam in human plasma by capillary electrophoresis. *J Chromatogr B Biomed Sci Appl*., 1997; 692(2): 483-487.
24. Lengyel J, Klebovich I, Magyar K. New validated gas-chromatographic method for piracetam determination in plasma. *Pharm Pharmacol Commun*, 1997; 3: 455-459.

25. Alebić-Kolbah T, Hirsl-Starcević S. Determination of piracetam in serum by gas chromatography. *J Chromatogr,* 1990; 526(2): 556-561.
26. Louchahi K, Determination of piracetam in human plasma and urine by liquid chromatography. *J Chromatogr B Biomed Appl*, 1995; 663(2): 385-389.
27. Curticapean A, Imre S. New validated method for piracetam HPLC determination in human plasma. *J Biochem Biophys Methods*, 2007; 69(3): 273-281.
28. Doheny MH, O'Connell MT, Patsalos PN. A high-performance liquid-chromatographic microanalytical procedure for the rapid estimation of piracetam in plasma or cerebrospinal fluid. *J Pharm Pharmacol*, 1996; 48(5): 514-516.
29. Nalbandian RM, Liquid-chromatographic quantification of piracetam. *Clin Chem*, 1983; 29(4): 664-666.
30. Rapid determination of piracetam in human plasma and cerebrospinal fluid by micellar electrokinetic chromatography with sample direct injection. *J Chromatogr B*., 2005.
31. Wang X, Determination of piracetam in rat plasma by LC-MS/MS and its application to pharmacokinetics. *Biomed Chromatogr*, 2010; 24(10): 1108-1112.
32. El-Gindy A, Emara S, Mostafa A. Spectrophotometric and LC determination of two binary mixtures containing antihistamins. Farmaco, 2004; 59(9): 713-722.
33. El-Saharty YSI. Simultaneous determination of piracetam and vincamine by spectrophotometric and high-performance liquid chromatographic methods. J AOAC Int., 2008; 91(2): 311-321.
34. Dhoru MM, Surani S, Mehta P. UV-spectrophotometric methods for determination of citicoline sodium and piracetam in pharmaceutical formulation. Der Pharmacia Lettre, 2012; 4(5): 1547-1552.
35. Sivadas A, Sathi A, Sathi K, Rahate KP. Development and validation of spectrophotometric methods for simultaneous estimation of citicoline and piracetam in tablet dosage form. J Pharm Bioallied Sci., 2013; 5: 202-207.
36. Hadad GM, Abdel-Salam RA, Emara S. Optimized and validated flow-injection spectrophotometric analysis of topiramate, piracetam and levetiracetam in pharmaceutical formulations. Acta Pharm, 2011; 61(4): 377-389.
37. Mittal A, Parmar S, Gilani SJ, Imam SS, Taleuzzaman M. Optimization and validation for simultaneous estimation of citicoline and piracetam in bulk and tablet formulations using RP-HPLC method: analytical quality by design approach. Asian J Res Chem, 2017; 10(2): 198-205.
38. Acharya M, Jain AK, Sharma N, Jain S, Saluja GS, Dixit A. RP-HPLC method development and validation for simultaneous determination of citicoline and piracetam in pharmaceutical dosage form. Indo Am J Pharm Res, 2015; 5: 3639-3647.
39. Panda SS, Ravi Kumar BVV, Mohanta G, Panda J. Reverse phase ultra fast liquid chromatography method for simultaneous estimation of citicoline sodium and piracetam in tablets. Int J Pharm Sci Nanotechnol, 2013; 6: 1952-1957.
40. Navaneethan G, Karunakaran K, Elango KP. Stability indicating and simultaneous determination of cinnarizine and piracetam from capsule dosage form by reversed phase high performance liquid chromatography. Indian J Chem Technol, 2013; 20(5): 323-326.
41. El-Houssini OM, Zawilla NH, Mohammad MA. Development and validation of RP-LC method for the determination of cinnarizine/piracetam and cinnarizine/heptaminol acefyllinate in presence of cinnarizine reported degradation products. Anal Chem Insights, 2013; 8: 99-106.

42. Ahmed AB, Abdelrahman MM, Abdelwahab NS, Salama FM. Stability-indicating TLC-densitometric and HPLC methods for the simultaneous determination of piracetam and vincamine in the presence of their degradation products. J AOAC Int., 2016; 99(6): 1490-1498.
43. Abdelrahman MM, Ahmed AB, Omar MA, Derayea SM, Abdelwahab NS. Development and validation of stability indicating chromatographic methods for simultaneous determination of citicoline and piracetam. J Sep Sci., 2020; 43(15): 2981-2988.
44. Siddiqui FA, Sher N, Shafi N, Sial AW, Ahmad M, Mehjebeen, et al. Development of new method for simultaneous analysis of piracetam and levetiracetam in pharmaceuticals and biological fluids: application in stability studies. Biomed Res Int., 2014; 2014: 758283.
45. Mansour NM, El-Sherbiny DT, Ibrahim FA, El Subbagh HI. Validation of a specific reversed-phase HPLC method for the quantification of three racetams: piracetam, levetiracetam, and brivaracetam in the presence of co-administered drugs in their pharmaceuticals; greenness assessment and application to biological fluid and in-vitro dissolution testing. Microchem J., 2022; 181: 107703.
46. Attia KAM, El-Olemy A, Serag A, Abbas AEFA, Eid SM. Environmentally sustainable DRS-FTIR probe assisted by chemometric tools for quality control analysis of cinnarizine and piracetam having diverged concentration ranges: validation, greenness, and whiteness studies. Spectrochim Acta A Mol Biomol Spectrosc, 2023; 302: 123161.
47. Mendes GD, Zaffalon GT, Silveira AS, Ramacciato JC, Motta RHL, Gagliano-Jucá T, et al. Assessment of pharmacokinetic interaction between piracetam and L-carnitine in healthy subjects: piracetam and L-carnitine pharmacokinetic interaction study. Biomed Chromatogr, 2016; 30(4): 536-542.
48. Winblad B. Piracetam: a review of pharmacological properties and clinical uses. CNS Drug Rev., 2005; 11(2): 169-182.
49. Pharmacokinetics and bioequivalence evaluation of piracetam tablet in healthy Chinese subjects under fasting and fed conditions.
50. Summary of Product Characteristics - Piracetam (Nootropil). Health Products Regulatory Authority (HPRA), Ireland.
51. ScienceDirect Topics. Piracetam - an overview.
52. De Reuck J, Van Vleymen B. The clinical safety of high-dose piracetam—its use in the treatment of acute stroke. Pharmacopsychiatry, 1999; 32 Suppl 1: 33-7.
53. Alshammari TM. Post marketing surveillance of suspected adverse drug reactions through spontaneous reporting: current status, challenges and the future.
54. Prakash J, Sachdeva R, Shrivastava TP, Jayachandran CV, Sahu A. Adverse event reporting tools and regulatory measures in India through outcome of Pharmacovigilance Programme of India. Indian J Pharmacol, 2021; 53(2): 143-152.
55. The pattern of adverse drug reaction reporting at a regional pharmacovigilance center in North India: a retrospective observational study.
56. Central Drugs Standard Control Organization (CDSCO). *Drugs and Cosmetics Rules, 1945 – Schedule H (Prescription Drugs).* CDSCO – Drugs Rules, 1945
57. European Medicines Agency (EMA). *Piracetam – List of Nationally Authorised Medicinal Products*.