A REVIEW ON ANALYTICAL EXPLANATION OF CYCLIC GABA DERIVATIVE (PIRACETAM)

Sparsh Sharma[1#], Abhay Bhardwaj[1#*], Anuj Pathak[2], Surya Prakash[3], Deepti Katiyar[4], N.G. Rao[5] , Radhika Aggarwal[6], Parul Grover[7]

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Abstract

Piracetam belongs to the derivatives of GABA. It belongs to BCS Class I which are having high permeability and high solubility. Piracetam was first synthesized in 1964 at the Belgian pharmaceutical company UCB by Dr. Corneliu, This medication is used to treat cognitive disorders associated with ageing, dizziness. This drug was first chemical agents possess memory enhancing capacity also known as *nootropics* ("smart drugs" or "cognitive enhancers"), Piracetam present in combine forms with like, levetiracetam, birvaracetam. Aim of this review to study the different analytical estimations of Piracetam and comparison study with other drug molecule. It also offers a brief description of various works already done on Piracetam.

Keywords- Piracetam, Nootropics, Cognitive Disorders, HPLC

[1#,1#*,2,3,4,5,6,7]KIET School of Pharmacy, KIET Group of Institution, Delhi-NCR, Ghaziabad, U. P. India.
Email: [1#*]Abhay.bhardwaj@kiet.edu

Corresponding Author:
Abhay Bhardwaj[1#*]
[1#*]KIET School of Pharmacy, KIET Group of Institution, Delhi-NCR, Ghaziabad, U. P. India.
# Both authors contributed equally

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1. Introduction

Piracetam chemically known as ($C_6H_{10}N_2O_2$) belongs to class of GABA. This medication, mainly used in the recovery related to memory forgetfulness in old people, seizure disorder, dizziness, Alzheimer's etc. [1-4] It is white or white crystalline powder, odorless with pka value is 15.67. It can be combined with citicoline, cinnarizine, levetiracetam, brivaracetam and carbamazepine. Various spectrophotometric techniques have reported the presence of Piracetam in bulk and pharmaceutical dosage form. [5] Piracetam being a GABA-derived neurotransmitter, has a wide range of cognitive reactions might be slightly partially due to the improvement in cell membrane adaptability. Piracetam has neuroprotective and anticonvulsant characteristics, enhances neuroplasticity and regulates neurotransmissions in a variety of transmittance systems (cholinergic). It seems to lessen erythrocyte adherence to vascular endothelium, prevent vasospasm, and promote microcirculation at the vascular level. Its usage in a variety of therapeutic reasons is consistent with this wide spectrum of physiological effects. [6] The Drug is categorized in BCS Class I, chemically which have high solubility and permeability. [7] The drug known to cause side effects such as psychomotor agitation, dizziness, memory loss, diarrhea, weight gain.

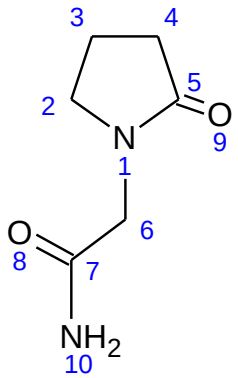

Fig 1. Chemical Structure of Piracetam

Drug Profile of Piracetam
Name- Piracetam
Molecular Formula-$C_6H_{10}N_2O_2$
Molecular weight- 142.156 g/mol
Category- Nootropics
Identification- By HPLC, UV-VISIBLE and HPTLC
Solubility- Soluble in water, methanol, ethanol, acetonitrile
Description- white or white crystalline powder.
Half-life- Approx. 5 hrs.
Use- Piracetam is a medication utilized in cure of Alzheimer's disease, dementia,
Adverse Effects- Diarrhea, Weight gain, Nausea

2. Various Analytical Methods

Analytical development is a related set of tasks in which test methods are created and qualified to support drug development phases. These methods evolve alongside the project, beginning with early discovery and progressing to commercial manufacturing. A plan for ensuring the identity, potency, and purity of the drug product or the composition and characterization of a formulated drug

product is developed following the determination of the critical quality attributes of the drug by analytical development. Choosing testing methodologies and demonstrating that they adhere to legal requirements and are appropriate for the intended use are all steps in the process. [8]

Development and validation of RP-HPLC procedure for piracetam

A quick, simple, and validated HPLC procedure was created to estimate the presence of piracetam in tablet 0.8 ml/min of isocratic flow rate was maintained. The C18 column was utilized and as (CH_3OH: H_2O) (20:80) main solvent, and the assessment was done at 205 nm. Concentration ranges from 2-14ug/ml. The retention time of Piracetam was 4.84 min and also the result showed that LOD and LOQ were 0.16 and 0.46ug/ml. The validated technique was established in compliance with ICH guidelines. The approach discovered found as straightforward, correct, and precise. [9, 10]

Simultaneously development and determination of piracetam and cinnarizine capsule formulation via RP-HPLC

Piracetam and cinnarizine drugs were simultaneously assessed utilizing a stability-indicating RP-HPLC assay procedure in a capsule dosage form. Isolation was gained by utilizing an octyl carbon column with a solvent mixture of (A) consisting of 0.015M K_2HPO_4 and 2ml of $N(CH_2CH_3)_3$ maintained at pH 6.0 with H_3PO_4 and C_2H_3N (90:10) and solvent mixture (B) containing 2 ml H_3PO_4 in 1000 ml, C_2H_3N and flowing run of 0.6ml/min^{-1}. The reverse phase for Piracetam was 11 minutes and 51 minutes for CN. The assessment was observed by a diode array UV-Vis detector at 205 nm. For simultaneous determination of the two drugs from the capsule, the suggested procedure was found to be specific, and linear. [11]

HPTLC validation of combination dosage formulation of citicoline sodium and piracetam

An easy, correct, HPTLC procedure for simultaneous assessment of citicoline sodium and piracetam as bulk and also for combination dosage forms has been created. A solvent of CH_3OH: H_20 was utilized in the process of the verification procedure. Aluminum plate coated with the silica Gel 60 F_{254} utilized in the form of the stationary phase. Densitometric assessments of the dissociated band were carried out at 212 nm. Verified procedure was linear in concentrations ranges of 400 to 3600 ng/spot of citicoline sodium and piracetam correspondingly. The precision procedure, is assessed by inter-day and intraday relative standard deviation. Interday and intraday peak outcome of relative standard deviation of citicoline sodium and piracetam are 0.62, 1.05% and 1.44, 1.06% respectively. Accuracy, assessed in respect of percentage recovery at 3 levels. Outcomes for citicoline sodium 97.66, 9.70% and 97.91% and for piracetam: 98.52, 97.61% and 96.64% correspondingly. Specification, assessed by spectral analysis of Citicoline sodium and Piracetam and overlapping the standards spectra and sample spectra correspondingly. [12]

Validation and assessment of piracetam in pharmaceutical using quantitative NMR spectroscopy

For the purpose of determining Piracetam, a straightforward correct proton NMR spectroscopy (^{1}H-NMR) procedure, was put forth and was approved. Deuterium oxide was used as the diluent and maleic acid served as the internal standard. Piracetam was quantified using NMR signal at 3.94ppm and 6.25ppm for the proton of piracetam and maleic acid. The procedure performance verification metrics, including linearity and others more

adequately met our needs. Linearity ranges (10-50 mg/o.6 ml) of D_2O and a correlation coefficient of 0.999. This procedure was the original one to use quantitative NMR spectroscopy to assess piracetam in pharmaceutical dosage forms and in bulk forms [13].

Indicating-stability TLC-densitometry and HPLC procedure in the simultaneous estimation of piracetam and vincamine in the presence of their degraded product

In parallel evaluations of piracetam and vincamine dosage formulations, as well as the appearance of and C, worsened outcomes, piracetam and vincamine respectively, a newly developed TLC-densitometric and RP-HPLC approach was developed, and verified. The suggested densitometric TLC approach is based on the quantification and dissociation of the tested chemicals on TLC silica gel 60 F254 plates using a generating system composed of CH_3CL-CH_3OH-CH_3OOH-$N(CH_2CH_3)_3$ (8+2+0.1+0.1v/v/v/v), and assessment was then performed (230nm). On the other hand, the developed RP-HPLC process is based on a constant concentration of the mobile phase of 0.05 M KH_2PO_4 (containing 0.1 percent tri-ethylamine maintained at pH 3 containing H_3PO_4)-CH_3OH (95+5v/v) on a C8 column and flowing run at (1ml/min) with assessment (230nm). The created procedure was verified using guidelines from the ICH. Furthermore, created TLC-densitometric and RP-HPLC procedures could be utilized as the indicating–stability assay procedures in the estimation of piracetam and vincamine simultaneously as bulk powders or dosage formulation. [14].

RP-HPLC procedure creation as well as verification in simultaneously determining the piracetam as well as mecobalamin as bulk and pharmaceuticals formulation

In the simultaneous detection of piracetam and mecobalamin tablet formulations, a novel, quick, isocratic RP-HPLC procedure has been created. Separation was achieved through a column Phenomenex C18, a main solvent consisting of pH 6.0 PO_4^{3-} buffer and C_2H_3N and CH_3OH in a (40.50.10) v/v/v ratio. The flowing run (1.0ml/min), and temperature of the column oven (25°c), and the temperature of the sample cooler was 25°c, and the volume of the injection (20L), an assessment carried out (215 nm) utilizing a photodiode array detector. Linearity was assessed for piracetam over the concentration ranges of 20.0-80.0g/ml as well as 0.025-0.10g/ml for mecobalamin. The Coefficient Correlation of piracetam was obtained to be 1.000 and mecobalamin was obtained to be 1.000. Piracetam has a relative standard deviation of 0.11% and Mecobalamin had a relative standard deviation of 0.03%. Piracetam had an intermediate precision of 0.12 % and mecobalamin had an intermediate precision of 0.78%. The accuracy for Piracetam was presented as percentage recovery at 50 to 150% levels. The percentage recovered limits are displayed as 100.01 to 100.74% and the findings received were found to be in limitation. As a result, the procedure discovered was obtained accurately. For mecobalamin, accuracy analysis was presented in percentage recovery at 50 to 150% levels. The maximum percentage recovery was 99.89 to 100.60%, and the outcomes were determined. Consequently, the accuracy of the procedure was confirmed. The procedure was verified in accordance with ICH guidelines. Suggested procedure found as repeatable, as well as constant. [15]

Verification of RP-HPLC indicating-stability in the simultaneous determination of citicoline and piracetam-containing tablets formulations

In the simultaneous detection of citicoline and piracetam in their synthetic combination as well as in combination with tablet composition, a dependable, as well as indicating- stability RP-HPLC procedure

was created. Two drugs were separated utilizing a chromatopak C18 column loaded with 10m particles. The rate of flow was 0.8 ml/min, and the main solvent (90:10) combination contain 10 mM K_3PO_4 buffer. UV assessment was performed at 215nm. The procedure shows adequate linearity with R (2) = 0.999 and (n = 3), correspondingly, and concentrations range of (17.5-32.5g/ml) Citicoline and (28-52 g/ml) Piracetam. The procedure proved to as reliable, withstanding subtle intentional changes to rate of flow, pH and mobile phase combination. By accurately detecting, the drug content of commercial pharmaceutical formulations, the procedure's usefulness was determined. [16]

RP-HPLC procedure creation and verification of simultaneous estimation of piracetam as well as vinpocetine

A verified RP-HPLC procedure for the simultaneous detection of piracetam and vinpocetine combination was developed. The C18 column is used & separation and analysis were carried out. The KH_2PO_4 buffer (0.05m, pH 6.0): CH_3OH (50:50, v/v) selected in the form of the main solvent, a flow rate (1.0 ml/min). For analyte detection, the wavelength was 225nm. For PIRA and VINP, the respective retention time of 3.52 mins and 7.41 mins were discovered. Over the concentrations ranges from (80-480 g/ml) of piracetam and (2-12 g/ml) of vinpocetine suggested method showed good linearity. For piracetam and vinpocetine, Correlation of coefficient values of 0.999 and 0.996, respectively, were discovered. The verification for this procedure, ICHQ2 (r1) guideline was obeyed. Vinpocetine and piracetam had recovery percentages of 101.38 0.71 and 102.04 0.58% respectively. The procedure's relative standard deviation was not determined to be greater than two, indicating that it was a precise one. The developed procedure for the simultaneous detection of PIRA and VINP was exact, accurate, reliable, selective, and quick. The analysis of a proprietary bi-layered tablet formulation was then conducted using the optimized methodology [17].

Liquid-Chromatographic Quantification of Piracetam

Piracetam absorb maximum at 197 nm. Its molecular absorption at 208 nm and pH 4.5 is 3576 (SD 251) L moI cm1. Some additional compounds absorbs in the range of (190 and 220 nm) due to C-N bonds, direct quantification at 197nm for piracetam in biological extract is difficult. 0.2m mol of piracetam per liter can be detected and quantified using chromatography of CH_3OH extract of serum and aqueous humor on a c-18 column created isocratically with KH_2PO_4 (0.1mol/L, pH 4.8). In these situations, the retention time of piracetam is 5 mm. The responses are linear for valves in the range of 5 and 15 nmol. The procedure was expensive but quick, and suitable for the clinical laboratories. [18]

Method development for piracetam as bulk and in pharmaceutical dosage form

A novel UV spectrophotometry procedure was created and verified in determination of piracetam in bulk and dosage formulations. The CH_3OH was used as a diluent in this technique. The first order derivative spectral were obtained at n=5, spectral width=2.0 nm, and measurements were obtained at 214 nm. In the presence of formulation excipients, the method demonstrated high specificity and adequate linearity containing concentrations ranges between off (10-80 g/ml). Intra and interday precision data shows, procedure which is highly reproducible. Accuracy was evaluated as well, with satisfactory outcome (mean recovery of 99.35%). The procedure was proven as correct, précised, and reproducible, and as well as used in routinely estimation of piracetam, both in bulk and in formulations. The method is verified in compliance with ICH guideline. [19]

Quantitative Analysis of Cinnarizine and Piracetam in Capsule Forms Using HPLC Method

A fresh isocratic HPLC procedure was created for the evaluation and dissociation of cinnarizine and piracetam at their purest forms and as well as their pharmaceuticals formulation. Hypersil Hold C18 column was utilized for separation. The effects of pH and main solvent as well as flowing run, was examined, calibration performed containing the range (10-80) g/ml) for cinnarizine and (160-960 g/ml) range having piracetam. For simultaneously determining of drugs in bulk and pharmaceuticals form this procedure was used, and procedure was approved using ICH parameters. [20]

Use in stability research of a novel method for simultaneously piracetam and levetiracetam estimation containing dosage form and biological fluid

The simultaneous quantification of Piracetam and Levetiracetam using RP-HPLC ultraviolet detection was created and verified. Chromatography performed on a nucleosil c18 column main solvent (70:30 v/v) combination of N $(CH_2CH_3)_3$and C_2H_3N at 0.1 g/l. The main solvent flow of rate maintained at (1ml/mn) as well as (λ-205nanometer). This method repeatability and specificity for quantifying of piracetam, levetiracetam, and as well as any contaminants were qualified using statistical parameters, demonstrating stability-indicating characteristics. The suggested procedure is extremely crucial because it allows for the dissociation of the primary component piracetam from levetiracetam. Both drugs showed continuous properties at ranges (20ng/ml and 10000 ng/ml). The LOQ (9.3and 8.7) and LOD (2.43and 1.66) of both drugs were determined. [21]

Piracetam determination in plasma by newly verified GC procedure

For assessment of the amount of piracetam, inside of the humans as well as in rat plasma, a verified GC procedure was developed. Tripelennamine was utilized as an internal control. Piracetam was detected using a nitrogen-phosphorus detector and separated using a fused silica capillary column. Piracetam-treated human and rat plasma specimens were processed for gas-chromatographic examination utilizing a rapid and easy Liquid-Phase extraction augmented along protein elimination. Considered Parameters was discovered in the range of the allowable limits. Piracetam decomposition was not observed in plasma samples stored at -20°C for six weeks. The calibration curves were Linear ranges (0.1to100 g/0.5 ml) plasma. The test was enough precise in the estimation of blood level following the regular everyday dosage of Piracetam. LOQ of piracetam was (0.1 um/0.5ml in plasma, as well as the LOD found to be less than the previous value (0.01 um/0.5ml). [22]

Piracetam determination method using High Performance Liquid Chromatography and microanalysis in plasma or cerebrospinal fluid

The Currently used GC and HPLC procedures for piracetam estimation requires vast samples and have interference issues. A micro- scale, isocratic HPLC procedure for determining piracetam in plasma (25L) or cerebrospinal fluid (10L) utilizing UV absorbance's (215nm) is described. Quantization limits (four micrograms ml^{-1}) and same-lot and different-lot coefficients of variance is minimum< 10%. Intervention was not found which further oftenly recommended anti-myoclonic is or antiepileptic drugs, so the procedure can be further be useful for monitoring of piracetam in patients on poly-therapy anti-myoclonic or antiepileptic medications. [23]

Novel techniques for cinnarizine detection by spectro-densitometry, spectro-photometry, and liquid chromatography in combination with piracetam

Four unique approaches were developed and verified to determine Cinnarizine HCL with combination with Piracetam in pure as well in dosage form. The first was a densito-metric analyzation, which offers quick as well as easy way to separate and measure cinnarizine HCL. The second procedure involved determining the drug through a colorimetric process that makes use of the reaction between 3-methylbenzothiazolin-2-one and an oxidant such as $FeCl_3$. With a signify accurateness of 100.10+/- 1.13p%, the green hue of the finished outcome was studied at 630nm, concentrations ranges (10-40 gram/ml). Cinnarizine H_2So_4, determined using the third method by direct spectrophotometric analysis at 252nm in the concentration ranges of 7–20 g/ml, on the other hand piracetam was found using derivative ratio spectro-photometry at 221.6 nm in the concentrations range of (5–30 gram/ml), signify accurateness of 100.14 0.79 and 100.26 1.24%, consecutively. Final procedure was the liquid chromatography estimation of cinnarizine h_2so_4 and piracetam, as per quantization estimation of chromatogram of cinnarizine H_2So_4 and piracetam (252 as well as 212 nm), correspondingly, at concentrations ranges of 10-200 g/ml for cinnarizine H_2SO_4 and (20-500 g/ml) for the piracetam, signify accurateness of 100.03 0. The suggested methods were tested using lab-created compositions and beneficially employed for the examination of their pharmaceutical composition. The effectiveness of the suggested method was furthermore evaluated by using the basic addition method. [24]

Piracetam and Its 4 contaminations determination by RP-HPLC with UV determination

Using quick, easy HPLC procedure, piracetam and its 4 contaminants, $C_6H_9NO_3$, C_4H_7NO, $C_7H_{11}NO_3$, and$C_8H_{13}NO_3$, separated and identified. A C18 column was utilized in isolation. A solution having ratio of $(CH_2CH_3)_3$-CH_3CN (85:15v/v) serves as mobile phase. The pH (6.5) of the main solvent was maintained by adding H_3PO_4 and the flowing run of 1 ml/min and using UV absorbance (205 nm). Created technique, discovered as effective in isolating pure drug from 4 associated constituents related to drug. The calibration plot polynomial regression data demonstrated a satisfactory linear relationship with r(2) = 0.9999 in the concentrations ranges from 50-10,000 ng/ml, 25-10,000 ng/ml, 45-10,000 ng/ml, 34-10,000 ng/ml, and 55.10,000 ng/ml, correspondingly. Procedure, verified in accordance with the guideline .Significant amount of piracetam were found to be 50 ng/ml, 25 ng/ml of $C_6H_9NO_3$, 45 ng/ml of C_4H_7NO, 34 ng/ml of $C_7H_{11}NO_3$, and 55 ng/ml of $C_8H_{13}NO_3$. Statistically estimation shows procedure is repeatable as well as particularly useful in estimating piracetam and its associated constituents. Because procedure successfully separated the drug from the associated constituents, it can be considered for stability indicator. The suggested procedure is highly efficient in separating the major constituent piracetam through the various variant impurities [25].

3. Conclusion

Piracetam is considered the most significant class of GABA derivatives, according to a literature review. This study came to a conclusion regarding the various analytical techniques, including HPLC, HPTLC, gas chromatography, and UV spectroscopy**.**

Abbreviations
C – Column
HPTLC – high performance thin layer chromatography
HPLC – high performance liquid chromatography
RP-HPTLC- reverse phase high performance thin layer chromatography
UV – Ultraviolet
GC – Gas Chromatography
PIR -Piracetam

VINC-Vincamine
VINP-Vinpocetine
LOD –limit of detection
LOQ – limit of quantitation
ICH– international council for harmonization
RP- reverse phase
RT- retention time

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