

Analytical Method Development and Validation of Gabapentin, Sodium Valproate and Fluvoxamine in Pharmaceutical Dosage Forms: A Review

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ABSTRACT

Gabapentin, sodium valproate, and fluvoxamine maleate are well-established central nervous system (CNS) medications, used respectively for epilepsy, neuropathic pain, bipolar disorder, and obsessive-compulsive disorder. Routine quality assurance for these drugs relies on dependable, validated analytical procedures, yet each compound presents distinct analytical difficulties: gabapentin and valproate lack a strong chromophore, so they must be detected at low UV wavelengths or following derivatisation, while fluvoxamine maleate has good UV absorption but is unstable under hydrolytic, oxidative, and photolytic conditions. This review brings together 45 analytical studies published from 1992 to 2025 concerning the measurement of these three drugs in both bulk and dosage forms, employing techniques such as UV-visible spectrophotometry, HPLC, HPTLC, GC, and LC-MS/MS. For each drug, the review compares chromatographic parameters, detection wavelengths, linearity ranges, and validation results, alongside stability-indicating and multi-component assay methods. General trends in method development, validation practices, and common shortcomings found in the literature are examined, along with suggestions for future research, including the adoption of greener solvents, UHPLC, and mass spectrometric detection.

Keywords: gabapentin; sodium valproate; fluvoxamine maleate; RP-HPLC; UV spectrophotometry

1. INTRODUCTION

Analytical methods are essential for the quality control, identification and quantitative estimation of pharmaceutical drugs in bulk and dosage forms. Among the various techniques, UV-visible spectrophotometry and RP-HPLC are widely employed because of their simplicity, accuracy, sensitivity and suitability for routine analysis^[1-3]. Analytical method development involves optimization of parameters such as solvent/mobile phase, pH, wavelength, flow rate, retention and resolution, while method validation confirms the reliability of the developed procedure through parameters such as specificity, linearity, accuracy, precision, LOD, LOQ and robustness^[1,2,4-8].

Gabapentin, sodium valproate and fluvoxamine maleate are important CNS-active drugs used in the management of neurological and psychiatric disorders. Due to their different chemical and physicochemical properties, their analytical estimation requires suitable and reliable analytical procedures. Several spectrophotometric and chromatographic methods have been reported for these drugs in bulk and pharmaceutical dosage forms. Therefore, this review summarizes the reported analytical methods, compares their analytical conditions and validation characteristics, and highlights their advantages, limitations and future scope.

UV-visible spectrophotometry is a simple and economical technique, but its specificity is limited. Therefore, it is mainly used for single-component dosage forms or mixtures having well-separated spectra ^[10–12,27]. For non-chromophoric drugs, derivatization reactions such as Schiff-base formation, diazotization and ninhydrin reactions can be used to improve detection ^[17,18,32,47]. RP-HPLC with UV or PDA detection is the most commonly reported technique. Important chromatographic parameters include efficiency, retention, selectivity and resolution, which determine the quality of separation ^[1]. Proper optimization of these parameters helps to minimize interference and co-elution. HPTLC, GC and LC-MS/MS are also used for specific applications such as dosage-form screening, analysis of volatile related substances and sensitive bioanalysis ^[22,38,40,48]. The analytical methods reviewed were generally validated according to ICH Q2(R1) for parameters including linearity, accuracy, precision, LOD, LOQ and robustness ^[2,26,29,36]. Stability-indicating methods may additionally include acid, alkali, oxidative, thermal and photolytic degradation studies.

Gabapentin is 2-[1-(aminomethyl)cyclohexyl]acetic acid (C₉H₁₇NO₂; molecular weight 171.24). It is structurally related to GABA and exerts its therapeutic action mainly through binding to the $\alpha 2\delta$ subunit of voltage-gated calcium channels ^[13,20,32]. Since gabapentin lacks a strong chromophore, direct UV estimation generally depends on weak absorbance in the 210–220 nm region, while derivatization methods may be used for improved spectrophotometric determination ^[15,17,18,32].

Sodium valproate is the sodium salt of 2-propylpentanoic acid and is widely used as an anticonvulsant ^[14,37,46]. Due to the absence of an aromatic chromophore, it shows weak UV absorption above 210 nm, making spectrophotometric estimation relatively challenging ^[14,37,46]. Consequently, reported analytical methods include spectrophotometry, gas chromatography and mass spectrometric techniques for different analytical applications ^[38,40,47].

Fluvoxamine maleate is a selective serotonin reuptake inhibitor (SSRI) containing a trifluoromethylphenyl chromophore. Its UV-absorbing properties allow spectrophotometric determination, particularly in the 230–271 nm region ^[49,58]. Its functional groups also permit various colour-forming and derivatization reactions for analytical estimation ^[48,49,53]. The reported literature includes direct UV, visible spectrophotometric and chromatographic methods for its determination in pharmaceutical formulations ^[50,52–54].

2. METHODS FOR GABAPENTIN

Twenty-two analytical studies on gabapentin were reviewed, comprising spectrophotometric, HPLC and HPTLC methods, including single- and multi-component analysis and one method for topical gel formulation.

2.1 Spectrophotometric methods

Various spectrophotometric methods have been reported for gabapentin, including direct UV and derivatization-based methods. The reported analytical conditions and validation parameters are summarized in Table 1 ^[15,17,18,21,24,32].

Title	Name of Journal with year of Publication	Summary	Ref. No.
Development and validation of spectrophotometric method for determination of gabapentin in bulk and pharmaceutical dosage forms based on Schiff base formation with salicylaldehyde	Journal of Applied Pharmaceutical Science, 2019	UV–Vis (Schiff base with salicylaldehyde) Detection wavelength:403 nm Linearity: 6–100 µg/ml LOD/LOQ: 1.16 / 3.48 µg/ml	32
Analytical method development and validation of gabapentin in bulk and tablet dosage form by using UV spectroscopic method	International Journal of Pharmaceutical Analysis and Research, 2017	UV Solvent: Methanol Detection wavelength:216 nm Linearity: 10–60 µg/ml	28

Method development and validation of gabapentin and estimation of gabapentin tablets by UV spectroscopy	Global Journal of Pharmacology, 2015	UV Solvent: 0.1 N NaOH Detection wavelength:217 nm Linearity: 1.5–9 µg/ml	24
Development and validation of UV spectrophotometric method for estimation of gabapentin in pharmaceutical dosage form	International Journal of Chemical and Pharmaceutical Sciences, 2012	UV Solvent: Ethanol : Water Detection wavelength:265 nm	21
Development and validation of UV-spectrophotometric method for gabapentin in bulk drug and formulation	Asian Journal of Research in Chemistry, 2011	UV–Vis (diazotisation and coupling with α -naphthol) Detection wavelength:558 nm Linearity: 10–50 µg/ml	18
A sensitive UV spectrophotometric method for the determination of gabapentin	E-Journal of Chemistry, 2009	UV Detection wavelength:210 nm Linearity: 0.25–3.5 µg/ml	15

Table 1 : Spectrophotometric methods reported for Gabapentin

2.2 Single-component HPLC methods

Title	Name of Journal with year of Publication	Summary	Ref. No.
Method development and validation for the quantitative estimation of gabapentin in bulk form and marketed pharmaceutical dosage form by RP-HPLC	International Journal of Advanced Research in Medical and Pharmaceutical Sciences, 2020	RP-HPLC Column:SymmetryC18(250×4.6m), 5µm M.P:Acetonitrile:Water(70:30%v/v) Detection wavelength:240 nm Flow rate: 1.0 ml/min RT: 2.790 min Linearity:10-35µg/ml; recovery100.36 %	33
Method development and stability studies of gabapentin in bulk and pharmaceutical dosage form	International Journal of Pharmacy and Biological Sciences, 2018	RP-HPLC Column: Symmetry ODS C18 M.P:Acetonitrile:1.0%OPA(75:25% v/v) Detection wavelength: 218 nm Flow rate: 1.0 mL/min RT: 3.742 min	30
RP-HPLC method development for the quantification of gabapentin in formulations	The Experiment, 2012	RP-HPLC Column: Zodiac C18(250×4.6mm), 5 µm M.P:Methanol:Acetonitrile:OPA(65: 33:2%v/v) Detection wavelength: 216 nm Flow rate: 1.0 mL/min RT: 3.7 min	20
Validation of an isocratic HPLC assay of gabapentin in pharmaceutical formulations and stress test for stability of drug substance	Der Pharmacia Lettre, 2011	RP-HPLC Column:UltrasphereC18 (250×4.6mm) M.P:Water:Acetonitrile : Methanol : Phosphatebuffer(55:35:10:0.1% v/v) Mode: Isocratic Detection wavelength:210nm (PDA)	19

		Flow rate: 1.0 mL/min	
Development and validation of a new HPLC method for the determination of gabapentin	International Journal of Biomedical Science, 2009	RP-HPLC Column: Waters C18(150×4.6 mm), 5 µm M.P:Methanol:KH ₂ PO ₄ (20:80%v/v), pH 6.2 Detection wavelength: 275 nm Flow rate: 1.0 ml/min Applied to serum and plasma (in vitro)	16

Table 2. Single-component HPLC methods for gabapentin

Single-component RP-HPLC methods typically report retention times of 2.8–3.7 min, while combination methods may show 1.6–2.0 min close to the dead time of 150–250 mm columns and more susceptible to excipient interference [27,29,34]. Study [19] applied more comprehensive suitability criteria: ≥ 6000 plates, tailing ≤ 2.0 , RSD $\leq 1.0\%$, and resolution ≥ 1.5 from related compound A.

2.3 Multi-component methods

Most simultaneous-estimation studies involved fixed-dose combinations of gabapentin with nortriptyline or amitriptyline, methylcobalamin, lidocaine or pregabalin.

Title	Name of Journal with year of Publication	Summary	Ref. No.
A novel stability indicating RP-HPLC method development and validation for simultaneous estimation of gabapentin and lidocaine in topical gel formulation	African Journal of Biomedical Research, 2025	RP-HPLC(gabapentin+lidocaine) Column:SymmetryC18(150×4.6mm), 5 µm M.P:Buffer:Methanol(80:20%v/v), pH 6.9 Detection wavelength: 209 nm Flow rate: 1.0 mL/min RT GBP: 5.936 min RT lidocaine: 14.206 min	36
Method development and validation of gabapentin, methylcobalamin and their degradative products by RP-HPLC	International Journal of Research and Analytical Reviews, 2024	RPHPLC(gabapentin+methylcobalamin) Column:WatersC18(250×4.6mm), 5 µm M. P.: OPA : Methanol (50:50 % v/v) Detection wavelength: 275 nm Flow rate:0.8mL/min; column temperature 25 °C	35
Development and validation of RP-HPLC method for the simultaneous estimation of gabapentin and nortriptyline hydrochloride in bulk and tablet dosage form	Journal of Young Pharmacists, 2022	RP-HPLC (gabapentin + nortriptyline) Column: Phenomenex Luna C18 (250 × 4.6 mm), 5 µm M.P:0.2%TEA(pH5.5):Acetonitrile (50:50 % v/v) Detection wavelength: 210 nm Flow rate: 1.2 mL/min RT GBP: 1.96 min RT nortriptyline: 4.54 min Linearity: 200–1000 / 5–25 µg/mL	34
Simultaneous estimation of gabapentin and	Journal of Drug Delivery and Therapeutics, 2019	RPHPLC(gabapentin+methylcobalamin) Column: Inertsil C18 (150 × 4.6 mm), 5 µm M.P: Buffer : Acetonitrile (60:40 % v/v)	31

methylcobalamin in bulk and pharmaceutical dosage form by RP-HPLC		Detection wavelength: 264 nm Flow rate: 1.0 mL/min RT GBP: 2.7 min RT methylcobalamin: 4.13 min Linearity: 25–150 / 0.125–0.750 µg/mL	
Development and validation of novel RP-HPLC method for simultaneous estimation of gabapentin and amitriptyline hydrochloride in bulk and pharmaceutical dosage forms	International Journal of Applied Pharmaceutics, 2018	RP-HPLC (gabapentin + amitriptyline; forced degradation) Column: Shim-pack C18 (250 × 4.6 mm), 5 µm M.P: 0.05M KH ₂ PO ₄ (pH2.1): Acetonitrile (55:45 % v/v) Detection wavelength: 221 nm Flow rate: 1.0 mL/min; 25 °C RT GBP: 1.959 min RT amitriptyline: 4.221 min Linearity: 720–1680 / 24–56 ppm	29
Development and validation of RP-HPLC method for simultaneous estimation of gabapentin and nortriptyline hydrochloride in bulk and combined dosage form	World Journal of Pharmaceutical Research, 2015	RP-HPLC (gabapentin + nortriptyline) Column: Luna C18 (250×4.6 mm), 5µm M. P.: Water : Acetonitrile (60:40 %v/v) Detection wavelength: 255 nm (PDA) Flow rate: 1.2 mL/min RT GBP: 3.457 min RT nortriptyline: 4.728 min Linearity: 50–500 / 1–12.5 µg/mL	26
Development and validation of stability indicating RP-HPLC method for simultaneous determination of gabapentin and nortriptyline in pharmaceutical dosage form	International Journal of Pharmaceutical Research and Analysis, 2015	RP-HPLC (gabapentin + nortriptyline; stability-indicating) Column: Agilent C8(150×4.6 mm),5 µm M. P.: 0.1 M Ammonium acetate : Methanol (80:20 % v/v) Detection wavelength: 254 nm Flow rate: 1.0 ml/min RT GBP: 2.66 min RT nortriptyline: 3.58 min Linearity: 800–2400 / 20–60 µg/ml	25
Development and validation of analytical method for simultaneous estimation of gabapentin and nortriptyline hydrochloride in pharmaceutical dosage form	Journal of Pharmaceutical Sciences and Bioscientific Research, 2015	RP-HPLC and UV (gabapentin + nortriptyline) M. P.: Methanol : Acetonitrile : 0.028 M Phosphate buffer, pH 4.5 (35:40:25 % v/v/v) RT GBP: 1.61 min RT nortriptyline: 2.6 min UV: 214 nm (GBP) and 238.7 nm (nortriptyline); linearity 200–700 / 7–12 µg/mL	27
RP-HPLC method development and validation for simultaneous estimation of gabapentin and methylcobalamin in tablet dosage forms	International Journal of Pharmaceutical Research and Analysis, 2014	RPHPLC(gabapentin+methylcobalamin) Column: C18 M.P:0.1%OPA:Acetonitrile(55:45%v/v) Detection wavelength: 271 nm RT GBP: 2.5 min RT methylcobalamin: 3.08 min Linearity: 600–1800 / 1–3 µg/mL	23
Simultaneous HPTLC	International	HPTLC (gabapentin + pregabalin)	22

method for estimation of gabapentin and pregabalin	Journal of Pharmacy and Pharmaceutical Sciences, 2013	Stationary phase: Silica gel 60 F254 M. P.: Ethyl acetate : Methanol : Ammonia (6.0:4.0:0.1 % v/v/v) $r^2 = 0.993 / 0.992$ Recovery: 99.13–101.83 % / 99.00–101.00 %	
UV-Vis spectrophotometric method for estimation of gabapentin and methylcobalamin in bulk and tablet	International Journal of ChemTech Research, 2010	UV-Vis (ninhydrin reaction) Detection wavelength: 405 nm (GBP) and 351 nm (methylcobalamin) Linearity: 50–300 / 1–7 µg/mL	17

Table 3. Reported methods of gabapentin in combination with other drugs

The combination studies indicate three significant points. Firstly, a considerable dose difference between gabapentin and co-formulated drugs necessitated the different calibration ranges. The wavelengths of 254–271 nm were found to be more appropriate for co-formulated drugs, whereas 210–221 nm was found to be more appropriate for gabapentin [25,26,29,34]. Secondly, the variations in the LOD and LOQ may be related to the differences in a detection wavelength, baseline noise, and calculation procedures. Thirdly, only a few studies [25,29,35,36] provided stability-indicating capability by means of forced degradation studies. The topical-gel method [36] was also found to be applicable to more than just oral formulations. However, the retention time of 14.2 min for lidocaine indicates that there is still a scope for optimization.

3. METHODS FOR SODIUM VALPROATE

Eleven sodium valproate studies were reviewed. They comprised seven RP-HPLC or related liquid-chromatographic methods, one GC procedure, one LC-MS/MS bioanalytical method, one visible colorimetric method and one review article.

Title	Name of Journal with year of Publication	Summary	Ref. No.
RP-HPLC method development and validation of sodium valproate in pharmaceutical formulations	Omdurman Islamic University Journal, 2024	RP-HPLC Column: L1(C18)(250×4.6mm), 5 µm M.P: Buffer: Acetonitrile(35:65% v/v) Detection wavelength: 220 nm Flow rate: 1.0 mL/min RT: 3.35 min Linearity: 250–1500 µg/mL; recovery 98–102 %	46
New spectrophotometric visible (VIS) analysis to determine sodium valproate from tablets	Preprints.org, 2024 (not peer-reviewed)	Visible spectrophotometry Diazonium salt of α -naphthylamine, alkaline medium Detection wavelength: 386 nm Content: 98.5 % of 500 mg tablet	47
RP-HPLC method development and validation for valproate and valproic acid in bulk and pharmaceutical dosage form	Biochemical and Cellular Archives, 2024	RP-HPLC Column: Symmetry ODS C18 (250 × 4.6 mm), 5 µm M. P.: Acetonitrile : Methanol (65:45 % v/v) Detection wavelength: 256 nm	45

		Flow rate: 1.0 mL/min RT: 2.256 and 5.427 min Recovery: 101.3 % / 100.5 %	
Development and validation of analytical method for determination of valproate and valproic acid in bulk and pharmaceutical dosage form by using RP-HPLC	International Journal of Allied Medical Sciences and Clinical Research, 2023	RP-HPLC Column: Symmetry ODS C18 (250 × 4.6 mm), 5 µm M. P.: Acetonitrile : Methanol (65:45 % v/v) Detection wavelength: 256 nm Flow rate: 1.0 mL/min RT: 2.256 and 5.427 min Linearity: 6–14 and 18–42 µg	43
RP-HPLC stability-indicating method for simultaneous determination of sodium valproate, methylparaben and propylparaben in oral solution	Acta Chromatographica, 2022	RP-HPLC (stability-indicating) Column: Waters C18 (150 × 3.9 mm), 5 µm M. P.: 0.05 M KH ₂ PO ₄ (pH 3.5) : Acetonitrile (50:50 % v/v) Detection wavelength: 210 nm Flow rate: 1.5 mL/min Range: 50–150 % of target (2.88 mg/mL sodium valproate)	42
Analytical method validation for related substances in sodium valproate oral solution by gas chromatography	Future Journal of Pharmaceutical Sciences, 2021	GC-FID Column: DB-FFAP capillary (30 m × 0.53 mm), 0.5 µm Sample prep: heptane extraction Six related substances; r = 0.9998 Recovery: 92.4–100.4 %	40
Development and validation of stability indicating assay method using RP-HPLC for determination of antiepileptic drugs in presence of their degraded product	Bulletin of Environment, Pharmacology and Life Sciences, 2021	RP-HPLC (DAD; valproic acid + sodium valproate) Column: Fortis C18 (100 × 4.6 mm), 2.5 µm M. P.: Acetonitrile :0.1 % OPA, pH 2.7 (80:20 % v/v) Detection wavelength: 210 nm Flow rate: 0.7 mL/min RT VA: 1.537 min RT SV: 4.910 min Linearity:14.5–87/33.3–199.8 µg/mL	41
A validated reversed-phase HPLC method for simultaneous determination of five antiepileptic drugs used in the treatment of Lennox–Gastaut syndrome in their pharmaceutical dosage forms	Asian Journal of Pharmaceutical and Clinical Research, 2018	RP-HPLC (five drugs incl. valproic acid; lacosamide as internal standard) Column: Restek C18 (250 × 4.6 mm), 5 µm M. P.: Acetonitrile : Water, pH 3.3 (55:45 % v/v) Detection wavelength: 210 nm Flow rate: 1.0 mL/min Valproic acid linearity: 36–180 µg/mL	39
Bioanalytical method development and validation of valproate semisodium in human	International Journal of Pharmaceutical Quality Assurance, 2014	LC-MS/MS (human plasma) Column: Sunfire C18 (150 × 4.6 mm), 5 µm M. P.: Acetonitrile : 10 mM	38

plasma by LC-MS/MS		Ammonium acetate (80:20 % v/v) Detection: negative-ion MRM Linearity: 1.012–120.399 µg/mL; LLOQ 1.012 µg/mL	
Estimation of sodium valproate in tablet dosage form by RP-HPLC without prior derivatization: application to dissolution studies	International Journal of Pharmaceutical Sciences and Drug Research, 2009	RP-HPLC Column: Nova-Pak phenyl (150 × 3.9 mm), 4 µm M. P.: Acetonitrile : Buffer, pH 2.5 (30:70 % v/v) Detection wavelength: 210 nm Flow rate: 1.2 ml/min Linearity: 50–1500 µg/mL (r = 0.9999)	37

Table 4. Reported methods of sodium valproate / valproic acid

The literature on sodium valproate shows a balance between simplicity and selectivity. Detection at 210–220 nm is simple, but may be affected by interference from excipients and mobile-phase components. Study ^[42] improved selectivity by separating sodium valproate from preservatives and degradation products. Phenyl and C18 columns have also been used to improve retention and separation ^[37,41]. GC-FID and LC-MS/MS methods have been reported for impurity and plasma analysis, respectively ^[38,40]. A visible colorimetric method was also reported ^[47].

4. METHODS FOR FLUVOXAMINE MALEATE

Twelve studies on fluvoxamine maleate were reviewed, including five spectrophotometric methods, five RP-HPLC methods, three of which involved stability or forced-degradation studies, one fluorescence-HPLC method for bioanalysis, and one review article.

4.1 Spectrophotometric methods

Direct UV determination has been reported using 0.1 N HCl at 246 nm over 5–10 µg/ml, with $Y = 0.026x + 0.0803$ and $r^2 = 0.9999$ [51,56]. Another procedure used 10 M urea as a hydrotropic medium and measured at 271 nm over 5–25 µg/mL, avoiding organic solvents ^[50]. Visible methods have included ninhydrin–ascorbic acid condensation, cobalt thiocyanate complexation and sodium nitroprusside reactions ^[49]. Ion-pair complexes with bromocresol green, methyl orange and bromothymol blue have also been extracted into chloroform and measured around 410–420 nm ^[53].

Title	Name of Journal with year of Publication	Summary	Ref. No.
Analytical method development and validation of fluvoxamine maleate in bulk and its formulation by UV spectroscopy	International Journal of Multidisciplinary Research and Development, 2024	UV Solvent: 0.1 N HCl Detection wavelength: 246 nm Linearity: 5–10 µg/mL $Y = 0.026x + 0.0803$; $r^2 = 0.9999$	56
A new spectrophotometric method for the determination of fluvoxamine maleate in pure form and in pharmaceutical formulation	Journal of Applied Pharmaceutical Science, 2015	Visible (ion-pair complexes with BCG, MO and BTB; extracted into chloroform; phthalate buffer) Detection wavelength: 420, 420 and 410 nm Linearity: 2–16, 2–15 and 2–20 µg/mL	53
Development and validation of UV-spectrophotometric method for the estimation of fluvoxamine maleate	Indo American Journal of Pharmaceutical Research, 2013	UV Solvent: 0.1 N HCl Detection wavelength:	51

in bulk and pharmaceutical dosage form		246 nm Linearity: 5–10 µg/mL $Y = 0.026x + 0.0803$; $r^2 = 0.9999$	
Spectrophotometric methods for the assay of fluvoxamine using chromogenic reagents	E-Journal of Chemistry, 2010	Three visible methods: (A) ninhydrin–ascorbic acid (B) cobalt thiocyanate (C) sodium nitroprusside	49
Spectrophotometric estimation of fluvoxamine maleate in tablets using hydrotropic agent	International Journal of Pharmaceutical Quality Assurance, 2010	UV (hydrotropic solubilisation) Solvent: 10 M Urea Detection wavelength: 271 nm Linearity: 5–25 µg/mL	50

Table 5. Reported UV / visible spectrophotometric methods of fluvoxamine maleate

4.2 Chromatographic methods

Title	Name of Journal with year of Publication	Summary	Ref . No.
A new analytical method development and validation of RP-HPLC method for estimation of fluvoxamine in bulk and tablet dosage form	World Journal of Advanced Pharmaceutical Sciences, 2025	RP-HPLC Column: Shim-packC18 (250×4.6 mm), 5 µm M.P: Acetonitrile: Phosphate buffer, pH 4.5 Detection wavelength: 254 nm Flow rate: 1.0 mL/min RT: 3.66 min LOD/LOQ: 6.39/19.36 µg/mL; recovery 99.42–100.71 %	59
Development and validation of UV spectrophotometric RP-HPLC method for simultaneous estimation of fluvoxamine in tablet and bulk	The Academic, 2024	RP-HPLC and UV Column: Poroshell C18 (150×4.6 mm), 5 µm M.P: Acetonitrile: 0.1% OPA (80:20% v/v) Detection wavelength: 230 nm RT: 8 min Linearity: 2–30 µg/mL; recovery 99.34 % LOD / LOQ: 0.394 / 1.193 µg/mL	57
Development and validation of a reversed phase HPLC method for simultaneous estimation of clomipramine and fluvoxamine	Journal of Global Trends in Pharmaceutical Sciences, 2023	RPHPLC (clomipramine + fluvoxamine) Column: Inertsil C18 (250×4.6 mm), 5 µm M. P.: 0.05 M Phosphate buffer, pH 4.6 : Acetonitrile (30:70 % v/v) Detection wavelength: 255 nm Flow rate: 1.0 mL/min RT clomipramine: 2.399 min RT fluvoxamine: 3.907 min Linearity: 100–500 / 1–5 µg	55
Force degradation study and RP-HPLC method development for estimation of fluvoxamine maleate in tablet	International Journal of Pharmacy and Pharmaceutical Sciences, 2015	RP-HPLC (force degradation) Column: Hyperchrome ODS C18 (250×4.6 mm), 5 µm M.P: Methanol: Phosphate buffer, pH 2.5 (70:30 % v/v) Detection wavelength: 250 nm	52

		Flow rate: 1.0 mL/min RT: 5.94 min Linearity: 10–50 µg/mL; accuracy 99.62 %	
A stability indicating HPLC method for the determination of fluvoxamine in pharmaceutical dosage form	Iranian Journal of Pharmaceutical Research, 2015	HPLC (stability-indicating) Column: Nova-Pak CN M.P:50 m M K ₂ HPO ₄ (pH7.0) : Acetonitrile (60:40 % v/v) Detection wavelength: 235 nm Linearity: 1–80 µg/mL; CV<2 %	54
Determination of fluvoxamine in human plasma by high-performance liquid chromatography with fluorescence detection	Journal of Chromatography B, 1992	HPLC–fluorescence (plasma; dansyl chloride derivatives) Internal standard: nortriptyline Linearity: 10–1000 ng/mL QC recovery: 103–105 %	48

Table 6. Reported chromatographic methods of fluvoxamine maleate

Forced-degradation investigations ^[52,54] indicate that fluvoxamine is susceptible to acidic, alkaline, oxidative and UV stress, whereas the neutral solid is comparatively stable under visible light and dry heat at 50 °C. These findings are relevant when designing packaging and storage studies. Review ^[58] reports UV methods in the 230–246 nm region over approximately 2–30 µg/mL, HPLC procedures with detection limits as low as 0.394 µg/mL and spectrofluorometric detection close to 0.01 µg/mL in biological fluids. The large difference between reported HPLC LOD values, such as 0.394 µg/mL ^[57] and 6.39 µg/mL ^[59], indicates the need for more consistent analytical procedures.

5. RESULTS AND DISCUSSION

The detection wavelength depends on the drug's chromophore. Fluvoxamine is usually detected at 230–271 nm, while gabapentin and sodium valproate are detected near 210–221 nm or require derivatisation. Low UV wavelengths can increase interference from solvents, buffers and excipients. Therefore, pure solvents and placebo/degradation studies are important.

The stability-indicating quality of the methods was different. Forced-degradation studies were reported for fluvoxamine ^[52,54] and some gabapentin and valproate methods ^[25,29,35,36,42]. However, several methods did not include stress studies ^[20,26,33,34,46]. Specificity against related substances is especially important for gabapentin and sodium valproate, but only a few studies clearly tested it ^[19,40].

Many methods gave the first peak within 1.5–3 minutes ^[1,27,29,34]. Although this is useful for fast analysis, good retention and separation are more important. Methods taking 14 minutes or longer, such as ^[36], may be improved by gradient or column optimisation.

Most studies used HPLC-UV and reported recovery, repeatability and LOD/LOQ. However, robustness, solution stability and system-suitability limits were often missing. Broad linearity ranges, such as 200–1000 µg/mL for gabapentin, should be checked carefully at low UV wavelengths ^[34]. HPTLC, GC and LC-MS/MS were rarely used ^[22,40,38], while green analytical methods were limited but included acetonitrile-free solvents and hydrotropic solubilisation ^[35,50].

6. CHALLENGES AND FUTURE PERSPECTIVES

1. Green analytical chemistry: safer solvent systems, such as ethanol–water or methanol-based mixtures, can be examined instead of acetonitrile and chloroform. Hydrotropic or aqueous media may also lower solvent consumption in spectrophotometry, provided that appropriate greenness metrics are reported.

2. UHPLC and sub-2 μm columns: these may be evaluated to shorten analysis time while preserving sufficient retention and resolution, particularly for polar compounds such as gabapentin.
3. Alternative detection systems: charged-aerosol detection, evaporative light-scattering detection, and LC-MS can offer more universal or more selective detection for non-chromophoric drugs such as gabapentin and valproate, thereby reducing reliance on low-wavelength UV or derivatisation.
4. Stability-indicating validation: future studies should incorporate systematic stress testing, the identification of degradation products, and the assessment of relevant related substances for gabapentin and valproate.
5. Analytical quality by design: AQbD strategies that use design-of-experiments optimisation and a well-defined method operable design region can enhance method comprehension and robustness, consistent with current ICH Q14 and Q2(R2) principles.
6. New dosage forms: analytical procedures should also be adapted for topical gels, extended-release products, and in-situ forming systems, using methods compatible with dissolution testing^[36,37].

7. CONCLUSION

Validated analytical methods are available for gabapentin, sodium valproate, and fluvoxamine across multiple analytical platforms. For the routine analysis of marketed dosage forms, reverse-phase high-performance liquid chromatography (RP-HPLC) with UV detection remains practical and widely used. The primary analytical challenges are the weak chromophoric characteristics of gabapentin and sodium valproate, which restrict direct UV detection mainly to the range of 210–221 nm or necessitate derivatisation, and the chemical instability of fluvoxamine, highlighting the importance of stability-indicating methods. Future method development should focus more on specificity, stress testing, environmentally friendly solvents, reduced run times, and more selective detection.

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