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REVIEW ARTICLE
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A REVIEW OF THE DEVELOPMENT AND VALIDATION OF ANALYTICAL METHODS FOR ESTIMATION OF VORTIOXETINE HYDROBROMIDE AND LURASIDONE HYDROCHLORIDE

Riya Patel[1], Dr. Neha Tiwari[2]*, Dr. Pragnesh Patani[3]

[1]Department of Pharmaceutical Quality Assurance, Khyati College of Pharmacy.
[2*]Prof. & Head of Pharmaceutical Chemistry & QA dept., Khyati College of Pharmacy, Ahmedabad, Gujarat, India.
[3]Head of Pharmacology department, Khyati College of Pharmacy, Ahmedabad, Gujarat, India.
Corresponding Author: Dr. Neha Tiwari

***Corresponding Author:** Dr. Neha Tiwari
Email: tiwarin1707@gmail.com *Khyati College of Pharmacy, Palodia, Ahmedabad, Gujarat.

Abstract
Analytical method development and validation are fundamental to pharmaceutical quality control, ensuring the identity, purity and potency of drug substances and finished products. Vortioxetine hydrobromide, an antidepressant with multimodal action, and Lurasidone hydrochloride, an atypical antipsychotic, are both clinically important central nervous system agents. A broad range of analytical techniques from simple spectrophotometric assays to chromatographic and mass-spectrometric methods has been applied to their analysis in bulk drug, formulations and biological conditions. The aim of this review is to focus on update of method development and validation for vortioxetine and lurasidone, emphasizing UV spectrophotometry, RP-HPLC, UPLC, HPTLC, and LC–MS/MS. Comparative evaluation and future directions.

Keywords: Vortioxetine Hydrobromide; Lurasidone Hydrochloride; Analytical Method Development; RP-HPLC; LC-MS/MS; Stability-indicating methods.

Introduction:

Analytical methods serve as the backbone of pharmaceutical research and quality control, providing reliable means to identify, quantify, and characterize drug substances and their impurities. Validation of these methods is guided by International Council for Harmonisation (ICH) guidelines, which define essential parameters such as accuracy, precision, specificity, linearity, robustness, and detection limits[1]. Among the different categories of analytical procedures, stability-indicating methods hold particular significance, as they are designed to separate the API from its degradation products formed under stress conditions[2].

Vortioxetine hydrobromide is an antidepressant with a unique multimodal mechanism of action, involving both serotonin transporter inhibition and receptor modulation. It is clinically approved for the treatment of major depressive disorder and has been the subject of extensive analytical method development[3]. Lurasidone hydrochloride, an atypical antipsychotic used in schizophrenia and bipolar

depression, is similarly important, requiring robust analytical approaches for its estimation in bulk and formulations[4].

Given their therapeutic importance, researchers have reported a wide variety of methods for both drugs. Spectrophotometric techniques provide cost-effective preliminary assays, while (HPLC) remains the standard for regulatory analysis. More advanced techniques, such as LC–MS/MS, are widely employed in bioanalysis due to their sensitivity and selectivity[5]. This review organizes and evaluates reported analytical approaches for vortioxetine and lurasidone, compares their applicability, and highlights future perspectives for method development.Vortioxetine hydrobromide:

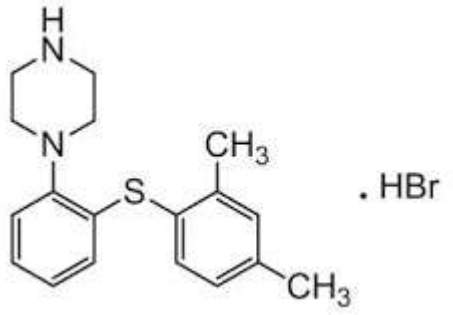

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Figure1: Chemical structure of Vortioxetine hydrobromide

FIELD	DETAILS
Drug	Vortioxetine hydrobromide
IUPAC name	1-[2-(2,4-dimethylphenylsulfanyl)phenyl]piperazine hydrobromide
Chemical Formula	C18H22N2S·HBr
Molecular mass	379.35 g/mol
Physical State	Solid (white to off-white powder)
Solubility	Freely soluble in water and methanol; sparingly soluble in ethanol
Therapeutic Use	Used in the treatment of major depressive disorder (MDD) as a multimodal antidepressant
pKa	~9.1 (basic, due to piperazine group)

Table 1: Drug Profile of Vortioxetine hydrobromide

Vortioxetine hydrobromide is a novel antidepressant approved for the treatment of major depressive disorder. It exhibits a multimodal mechanism, functioning as a serotonin transporter inhibitor and modulator of various serotonin receptor subtypes[7].

Several spectrophotometric methods have been developed for vortioxetine, useful for preliminary estimation in bulk and simple formulations[8]. These methods are fast and inexpensive, but they lack specificity, especially in the presence of impurities or excipients. Chromatographic approaches, particularly reverse-phase HPLC (RP-HPLC), are more commonly employed. Validated stability-indicating HPLC methods have been reported, capable of detecting degradation products under hydrolytic, oxidative, photolytic, and thermal stress conditions[9,10]. UPLC has also been explored to reduce analysis time and solvent usage[11,12] .

For pharmacokinetic and forensic purposes, LC–MS/MS has proven highly effective. Sensitive assays have been developed to quantify vortioxetine in plasma and biological matrices, supporting therapeutic drug monitoring and clinical pharmacology studies [13] . Forced degradation studies, combined with LC–MS/MS, have provided valuable insights into its degradation pathways and stability profile[14].

Lurasidone hydrochloride:

[15]

Figure 2: Chemical structure of Lurasidone hydrochloride.

Lurasidone hydrochloride is an atypical antipsychotic indicated for the treatment of schizophrenia and bipolar depression. Its pharmacological profile includes dopamine D2 and serotonin 5-HT2A antagonism, as well as partial agonist activity at 5-HT1A receptors.

Analytical methods for lurasidone include spectrophotometric approaches, suitable for preliminary analysis, and chromatographic methods such as RP-HPLC, which are widely applied for assay and stability-indicating studies [16,17]. Validated HPLC methods can separate the drug from its degradation products, ensuring reliability in quality control testing[18].

Advanced bioanalytical methods include LC–MS/MS assays for the quantification of lurasidone and its metabolites in plasma and biological samples. These methods are particularly important in pharmacokinetic and bioequivalence studies, where sensitivity and selectivity are crucial[19]. Forced degradation studies using chromatographic and LC–MS/MS approaches have further elucidated lurasidone's stability under acidic, alkaline, oxidative, and photolytic stress conditions[20].

FIELD	DETAILS
Drug	Lurasidone hydrochloride
IUPAC name	(1S,2R,6S,7R)-4-[[(1R,2R)-2-[[4-(1,2-benzothiazol-3-yl)piperazin-1-yl]methyl]cyclohexyl]methyl]-4-azatricyclo[5.2.1.0^{2,6}]decane-3,5-dione hydrochloride
Chemical formula	$C_8H_{36}N_4O_2S \cdot HCl$
Molecular mass	~ 529.14 g/mol
Physical state	Solid, white to off-white powder
Solubility	Very slightly soluble in water; practically insoluble in 0.1 N HCl; slightly soluble in ethanol; sparingly soluble in methanol; insoluble or practically insoluble in toluene; very slightly soluble in acetone
Therapeutic use	Treatment of bipolar depression; atypical antipsychotic

Table 2: Drug Profile of Lurasidone hydrochloride

Comparative discussion:

Analytical evaluation of central nervous system drugs such as vortioxetine and lurasidone has increasingly relied on validated chromatographic and combined techniques to ensure reliability, sensitivity, and reproducibility. Spectrophotometric approaches provide primary options but are limited by their lack of selectivity, particularly in complex formulations[21]. In contrast, reverse-phase HPLC methods remain the most widely used in quality control settings, offering robustness and compliance with ICH requirements[22]. For bioanalytical applications, liquid chromatography coupled with tandem mass spectrometry has emerged as the preferred technique, owing to its high sensitivity and ability to detect drugs and metabolites in biological matrices[23]. Stability-indicating methods are

critical for both compounds, as they enable detection of degradation products under forced stress conditions and provide assurance of long-term quality[24]. Recent developments also highlight the utility of advanced UPLC and LC-MS/MS platforms that reduce analysis time, improve resolution, and enhance overall quantity [25].

Table 3: Reported methods for Vortioxetine hydrobromide and Lurasidone hydrochloride

DRUG	METHOD	ANALYTICAL CONDITIONS	Application	REFRENCES
Vortioxetine hydrobromide	UV Spectrophotometry	λmax at 225 nm in methanol	Bulk and tablet dosage forms	[26]
Vortioxetine hydrobromide	RP-HPLC	C18 column, mobile phase acetonitrile: phosphate buffer, detection at 230 nm	Assay and impurity profiling	[27]
Vortioxetine hydrobromide	UPLC	C18 column, gradient elution, short run time	Stability-indicating assay	[28]
Vortioxetine hydrobromide	LC–MS/MS	Electrospray ionization, multiple reaction monitoring	Quantification in plasma for pharmacokinetics	[29]
Lurasidone hydrochloride	UV Spectrophotometry	λmax at 242 nm in methanol	Bulk and simple formulations	[30]
Lurasidone hydrochloride	RP-HPLC	C8/C18 column, acetonitrile: buffer, detection at 254 nm	Assay in tablets and impurity profiling	[31]
Lurasidone hydrochloride	Stability-indicating RP-HPLC	Forced degradation under acidic, alkaline, oxidative conditions	Stability studies in formulations	[32]
Lurasidone hydrochloride	LC–MS/MS	ESI interface, plasma extraction, MRM detection	Bioanalysis in plasma for pharmacokinetics	[33]

Conclusion:

The analytical evaluation of Vortioxetine Hydrobromide and Lurasidone Hydrochloride highlights the central role of validated methods in ensuring pharmaceutical quality, therapeutic efficacy, and patient safety. Preliminary UV spectrophotometric techniques serve as simple, cost-effective approaches for bulk and dosage form analysis, though they are limited by low specificity. Chromatographic methods, particularly RP-HPLC and UPLC, provide robust, accurate, and stability-indicating assays that comply with ICH guidelines and are widely adopted for quality control and impurity profiling. The incorporation of LC–MS/MS methodologies has significantly advanced bioanalytical applications, enabling sensitive detection of drugs and metabolites in plasma, which is critical for pharmacokinetic and therapeutic drug monitoring studies. Comparative evaluation of these approaches demonstrates that while simpler techniques are useful for routine screening, advanced chromatographic and mass-spectrometric methods remain indispensable for regulatory and clinical

applications. Stability-indicating studies further ensure the reliability of both compounds under forced degradation conditions, contributing to long-term product assurance. Future trends point toward the application of Quality by Design (QbD), green analytical chemistry, and hybrid platforms to enhance efficiency, sustainability, and reproducibility. Thus, the collective evidence emphasizes that a multi-tiered analytical strategy—ranging from spectrophotometry to LC–MS/MS—is essential for comprehensive evaluation of Vortioxetine Hydrobromide and Lurasidone Hydrochloride across preclinical, formulation, and clinical settings.

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