Review on Analytical Methods Reported for the Estimation of Antipsychotic Drugs- Paliperidone Palmitate, Dexmedetomidine, Xanomeline.

Nigar Parveen Siddiqui[1], Chimpiri Srujani[1]*, Himanshu Trivedi[2], Himanshu Kesharwani[3]

Department of Pharmaceutical Sciences, School of Pharmaceutical Sciences, Babasaheb Bhimrao Ambedkar University, Lucknow-226025, Uttar Pradesh, India

Corresponding Author*
Dr Chimpiri Srujani
Assistant Professor
Department of Pharmaceutical Sciences, Babasaheb Bhimrao Ambedkar University, Lucknow
Mobile: 9030779861
Email: srujani_dewdrops@yahoo.in

Abstract:

Method development in analytical techniques is essential to ensure accurate, precise, and reliable measurement of drug substances and formulations. It helps in optimizing the conditions for separation, identification, and quantification, ensuring quality control, regulatory compliance, and stability assessment of pharmaceutical products. This review focuses on the reported analytical methods used to estimate three important antipsychotic agents: paliperidone, dexmedetomidine, and xanomeline. These drugs, though diverse in their mechanisms and uses, require precise and validated analytical approaches for their detection in pharmaceutical formulations and biological samples. Various techniques, including HPLC, RP- UPLC, LC-MS/MS, and UV- visible spectrophotometry, are explored in terms of their effectiveness, sensitivity, and practicality. The review also discusses key factors involved in method selection, such as sample matrix, detection limits, and regulatory guidelines. By compiling and comparing existing methods, this review aims to guide researchers, analysts, and pharmaceutical professionals in choosing and developing appropriate analytical strategies for the estimation of these antipsychotic drugs.

Keywords: *Antipsychotic Drugs, HPLC, RP-UPLC, UV Spectrometry, HPTLC, LC-MS/MS.*

Introduction:

Formulating an analytical method involves establishing and enhancing a procedure to ascertain the chemical composition, concentration, or structure of substances inside a sample. This procedure entails choosing the best analytical methods, such as HPLC, UV Spectrometry, HPTLC, UPLC, LC-MS/MS etc. to figure out the ideal experimental setup and getting the sample ready for examination [1]. In HPLC, a liquid (mobile phase) is pushed through a porous material column (stationary phase) under high pressure after a sample solution has been introduced into the column. A distinct partition of the sample between the stationary and mobile phases results in variations in the rates of migration across the column, which serve as the basis for sample separation [2]. According to the RP-HPLC concept, the solute is attracted to the stationary phase and adsorbs onto it, resulting in separation [3] . HPLC is widely used in stability studies, *in-vitro* release studies, and bioequivalence studies to ensure the safety and efficacy of drug products. It is also applied for impurity profiling, assay of active ingredients, pharmacokinetic studies, and quality control of pharmaceutical formulations.

UPLC is based on HPLC, and its primary goal is to reduce particle size in a packing column, increasing efficiency and thus resolution. The foundation of the UPLC approach is the employment of a stationary phase made up of particles smaller than 2µm [4]. UPLC finds wide application in pharmaceutical analysis due to its high sensitivity and reduced run time. UPLC helps in analysing nutrients, additives, preservatives, flavour compounds, and contaminants, ensuring product quality and safety. Clinically and in forensic science, it is used for therapeutic drug monitoring, toxicology studies as well as in biotechnology for the analysis of proteins, peptides, and metabolites.

Ionizing chemical substances to produce charged molecules or molecule fragments and detecting their mass-to-charge ratios is the fundamental idea behind mass spectrometry. For the identification, measurement, and structurization of intricate biological and chemical samples, this method has become essential in contemporary analytical labs [5] .

The powerful analytical method known as HPTLC is effective for both quantitative and qualitative examination. Partitioning, adsorption, or both may be the source of separation, depending on the kind of adsorbents used on the plates and the solvent system used for development [6]. HPTLC is widely applied in qualitative and quantitative analysis of pharmaceuticals, herbal drugs, and natural products. It is used for stability studies, impurity profiling, and in-vitro release studies, as well as for the identification and fingerprinting of herbal formulations. In addition, HPTLC serves in quality control, purity testing, and pharmacokinetic studies, owing to its ability to analyse multiple samples simultaneously with high accuracy and reproducibility.

UV spectroscopy has both qualitative and quantitative analytical uses. One of the benefits of UV spectroscopy techniques is its low labor and time requirements [7] . The measurement of monochromatic light absorption by colorless substances in the near-ultraviolet range (200–400 nm) is the foundation of UV spectroscopy study [8] . UV spectroscopy is widely used in qualitative and quantitative analysis of drugs and pharmaceutical formulations. It is applied in stability studies, detection of impurities, and in-vitro dissolution/release studies. Additionally, UV spectroscopy is used for assay of APIs, kinetic studies, and quality control testing, owing to its simplicity, sensitivity, and cost-effectiveness.

Liquid Chromatography-Mass Spectrometry (LC-MS) is a potent analytical method that combines the high sensitivity and selectivity of mass spectrometry with the separation capabilities of liquid chromatography. The basic idea behind LC-MS is to use liquid chromatography to first separate complicated mixtures of compounds, and then mass spectrometry to identify and quantify those separated molecules based on their mass-to-charge ratio [9]. LC–MS is applied in proteomics, metabolomics, and biomarker discovery, as well as in toxicology, environmental analysis, and food safety testing, due to its high sensitivity, selectivity, and structural elucidation capabilities.

Paliperidone:

Paliperidone is an active byproduct of the atypical antipsychotic, Risperidone, classified within the chemical category of Benzisoxazole derivatives [10] . Paliperidone's molecular mass is 664.89 g/mol, and its chemical formula is $C_{39}H_{57}FN_4O$. Paliperidone has an antagonistic impact on H1 receptors as well as α1 and α2 adrenergic receptors. It is used to treat schizophrenia and other psychotic symptoms [11]. The US Food and Drug Administration (US-FDA) authorized it in December 2006 [12]. Paliperidone is almost soluble in H_2O, 0.1N Sodium Hydroxide, and C_6H_{14}, and weakly soluble in 0.1N HCL and methyl chloride.

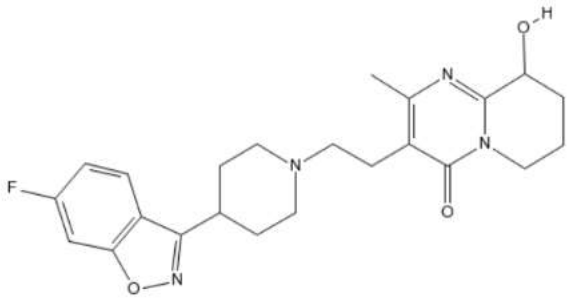

Figure 1. Structure of Paliperidone

Dexmedetomidine:

Dexmedetomidine is a strong and extremely selective α2 adrenoceptor agonist that has sedative, analgesic, and anxiety-reducing properties, which is used for patients admitted to the ICU [13] and belongs to the chemical class of lipophilic imidazole derivatives [14]. The chemical formula of dexmedetomidine is $C_{13}H_{16}N_2$, and the molecular mass is 200.28g/mol. The U.S. Food and Drug Administration (US-FDA) authorized it in 2022. In water, dexmedetomidine dissolves readily.

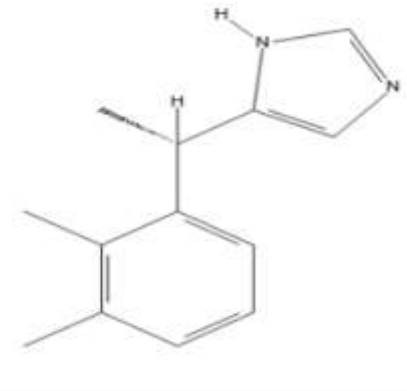

Figure 2. Structure of Dexmedetomidine

Xanomeline:

Xanomeline selectively binds to M1 receptors and is a potent muscarinic receptor agonist [15]. Xanomeline belongs to the thiadiazole and tetrahydropyridine chemical groups. Phase 1 clinical trials are presently being conducted on xanomeline tartrate to treat Alzheimer's disease. Targeting muscarinic receptors rather than dopamine receptors is the first authorized treatment for schizophrenia. Xanomeline's molecular mass is 281.42g/mol, and its molecular formula is $C_{14}H_{23}N_3OS$ [16]. The Food and Drug Administration (FDA) approved xanomeline and trospium chloride together in September 2024. Dimethyl formamide (DMF) is where xanomeline dissolves, and aqueous buffers only weakly dissolve it.

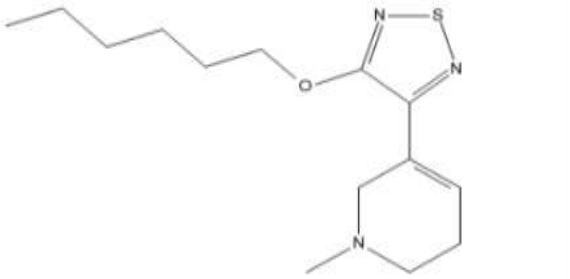

Figure 3. Structure of Xanomeline

Reported Analytical Methods for the selected Antipsychotic Drugs

Table 1. Reported Analytical Methods for Paliperidone

S.NO	METHODS	DESCRIPTION	RESULTS	REF NO.
1	Analytical method for estimation by HPLC	Stationary Phase: Phenomenex C18 column Mobile Phase: ACN: CH_3OH: KH_2PO_4 (pH-3) (45:30:25, %v/v) Wavelength: 275nm Flow Rate: 1ml/min	Linearity: 100-500 µg/ml Retention Time: 4.150 min Theoretical Plate: 3060 LOD:500ng/ml	[17]

		Run Time: 10min Injection Volume: 20µL	LOQ: 1µg/ml	
2	Stability indicating RP-UPLC in depot injectable formulation	Stationary Phase: BEH C18 Mobile Phase: $NH_4CH_3CO_2$: ACN (10:90 %v/v) Wavelength: 238 nm Flow Rate: 0.6ml/min Run Time: 2.5 min Injection Volume: 1µL Temperature: 50°C (column oven)	Linearity: 156-468 µg/ml Retention Time: 1.3 min Drug was found to be sensitive in oxidation condition with 21.7%w/w degradation	[18]
3	UV in bulk and their solid dosage form	Solvent: Dimethylformamide (DMF) Wavelength: 280nm	Linearity: 10-60µg/ml LOD: 1.82µg/ml LOQ: 6.07µg/ml Regression correlation coefficient r2=0.999	[19]
4	Stability indicating HPTLC in bulk drug	Stationary phase: Silica Gel-$60F_{254}$ Mobile Phase: $CHCl_3$:CH_3OH (3:7 v/v) Wavelength: 236nm	Linearity:500-2500ng/band LOD: 47.7ng/band LOQ:144.56ng/band RF Value: 0.54 ± 0.03 Regression correlation coefficient r2=0.984 Drug was found to be sensitive in acid, base, oxidation and thermal conditions.	[20]
5	HPTLC method for *in-vitro* release study	Stationary Phase: Silica Gel- $60F_{254}$ Mobile Phae: CH_3OH:$C_4H_8O_2$ (8:2 v/v) Wavelength: 284nm	Linearity: 100-600 ng/ml LOD: 15.11ng/spot LOQ:45.79ng/spot RF Value: 0.54 ± 0.011 Regression correlation coefficient r2=0.9997	[21]

6	Analytical QBD compliant ultrafast liquid chromatography for determination in extended-release tablet dosage form	Stationary Phase: C-18 (250 ×4.6mm, 5µm) Mobile Phase: CH_3OH: 10mM tetra butyl ammonium hydrogen sulphate (95:5 %v/v) Wavelength: 279nm Flow Rate: 1ml/min Run Time: 10min Injection Volume: 20µl	Linearity: 2-100 µg/ml LOD: 0.5µg/ml LOQ: 2µg/ml Retention time: 2.64min	[22]
7	Studies in OROS tablets- extraction procedure and chromatographic analysis by HPLC method	Stationary Phase: Shim-pack CLC ODS (250 ×4mm, 5µm) Mobile Phase: 50mM monobasic phosphate buffer containing 0.3% triethylamine: Acetonitrile (70:30 %v/v) Wavelength: 280nm Flow Rate: 1ml/min	Linearity: 10-50µg/ml Retention time: 4.8min Theoretical plates: 12634.21 Tailing factor: 1.31	[23]
8	A Validated stability indicating UPLC method for simultaneous determination of assay, related substance and degradation products	Stationary Phase: BEH C18 Mobile Phase: (A)20mM $KH_2PO_4{\cdot}H_2O$ and 1.5mL of triethylamine buffer (B) Water and Acetonitrile, (10:90 %v/v) Wavelength: 238nm Flow Rate: 0.5ml/min Run Time: 10min Injection Volume: 10µl Temperature: 35°C	Linearity: Retention Time: 4.649min LOD: 0.0001µg/ml LOQ: 0.0005 µg/ml Drug was found to be stable under light and heat, but susceptible to hydrolytic, acidic, basic, and oxidative degradation.	[24]
9	Development and Validation of UV Spectroscopic method	Solvent: 20% Methanol in Milli -Q-water λ_{max}:283nm	LOD: 0.03µg/ml LOQ: 0.10µg/ml Linearity:5-30µg/ml	[25]

Table 2. Reported Analytical Methods for Dexmedetomidine

S.NO	METHODS	DESCRIPTION	RESULTS	REF NO.
1	Development and Validation by HPLC	Stationary Phase: ODS 3V Mobile Phase: NaH_2PO_4 buffer pH 4.6 and ACN (80:20 %v/v) Wavelength: 215nm Flow Rate: 1.5ml/min	Linearity: 1.04-6.23µg/ml Retention Time: 8.451 min LOD: 0.0308 µg/ml LOQ:0.0933 µg/ml	[26]
2	Optimization and Validation of Spectrophotometric method in pure and dosage form	Solvent: N-Bromosuccinimide (NBS) Dye: Amaranth λ_{max}: 530nm	LOD: 0.0567 µgD/ml LOQ: 0.17182 µg/ml Linearity:2-9µg/ml %Recovery:99.75-100.25	[27]
		Solvent: N-Bromosuccinimide (NBS) Dye: Safranin λ_{max}: 530nm	LOD: 0.2274 µg/ml LOQ: 0.68407 µg/ml Linearity:4-11.5µg/ml %Recovery:99.1-99.83	
		Solvent: N-Bromosuccinimide (NBS) Dye: Analine Blue λ_{max}: 610nm	LOD: 0.0475 µg/ml LOQ: 0.14402 µg/ml Linearity:2-10µg/ml %Recovery:99.66-99.40	
		Solvent: N-Bromosuccinimide (NBS) Dye: Rhodamine B λ_{max}: 560nm	LOD:4.2556×10-4 µg/ml LOQ:1.2896×10-3 µg/ml Linearity:1.2-3.5µg/ml %Recovery:98.88-99.0	
3	Stability indicating HPLC method validation for the assay in Dexmedetomidine HCL injection	Stationary Phase: LiChrospher, 100 RP-18 end capped, 4mm×12.5cm, 5µm Mobile Phase: 60-40% of methanol and Sodium	Linearity: 50-15 µg/ml Regression correlation coefficient r2=0.999 Retention time: 8min	[28]

		Phosphate dihydrate monobasic Wavelength: 220nm Flow Rate: 1ml/min Run Time: 15 min Injection Volume: 200µl		

Table 3. Reported Analytical Methods for Xanomeline

S.NO	METHODS	DESCRIPTION	RESULTS	REF NO.
1	Determination in Human Plasma by Ionspray Tandem Mass spectrometry	Stationary Phase: 10×1 mm Hypersil C-18 Mobile Phase: 33 mM $C_2H_7NO_2$ and 0.33% CH_3COOH in H_2O-ACN (30:70 %v/v) Flow Rate: 50 µL/min Run Time: 2.5min Injection volume:20 µL	Linearity: 0.075-5 ng/ml LOD: 1.5 ng/ml Xanomeline is detected at m/z value of 282	[29]
2	HPLC assay, a specific M-1 agonist, and its metabolite in human plasma	Stationary phase: Zorbax CN, 150x4.6 mm, 5- µm Mobile Phase: 0.5% (5 ml/l) of C_6H15_N (pH 3.0) with concentrated H_3PO4 oxolane in ratio of 70:30 %v/v Wavelength:296nm FlowRate:1ml/min Run Time: 25 min Injection Volume: 180µL	Linearity: 1.5-20ng/ml LOQ: 1.5ng/ml Retention Time: 10.8 min Desmethylxanomeline is the primary metabolite of xanomeline, formed via demethylation, and its quantification was necessary to fully assess the drug's pharmacokinetics in plasma during clinical trials.	[30]
3	Determination of Xanomeline and active metabolite N-desmethyl Xanomeline in Human	Stationary Phase: RP-8.30×4.6mm Mobile Phase: 1% TFA in H_2O-ACN (10:90 %v/v) Flow Rate: 1ml/min Run Time: 3min	LOQ of Xanomelin:75pg/ml LOQ of N-desmethyl Xanomeline: 200pg/ml Retention Time: 30s	[31]

<table>
<tr><td></td><td>Plasma by liquid chromatography-atmospheric pressure chemical ionization mass spectrometry</td><td>Injection Volume:50µL</td><td></td><td></td></tr>
<tr><td>4</td><td>Development and Validation by RP-HPLC for simultaneous quantification of Xanomeline and Trospium chloride in pharmaceutical dosage form</td><td>Stationary Phase: Kromasil C18
Mobile Phase: ACN and 0.1% HCOOH (40:60 %v/v)
Wavelength: 231nm
Flow Rate: 1ml/min
Run Time: 6min
Injection Volume: 10µL</td><td><table><tr><th>Xanomeline</th><th>Trospium Chloride</th></tr><tr><td>Linearity: 25-150 µg/ml</td><td>Linearity: 5-30 µg/ml</td></tr><tr><td>Retention time:2.422 min</td><td>Retention time: 3.385min</td></tr><tr><td>% Recovery: 99.7</td><td>% Recovery: 100.0</td></tr><tr><td>Xanomeline shows maximum degradation under peroxide (14.1%) and alkali (12.2%)</td><td>Trospium chloride exhibited significant degradation under peroxide(14 %) and acid(11.2%)</td></tr></table></td><td>[32]</td></tr>
<tr><td>5</td><td>Determination of Xanomeline (LY246708 tartrate) in rat and monkey plasma by capillary gas chromatography with nitrogen-</td><td>Stationary Phase: DB1701, 30m x0.25mm
Mobile Phase: Carrier gas (Helium)
Flow Rate: 4ml/min
Run Time: 26.1min</td><td>Linearity: 8-800ng/ml
LOQ: 8ng/ml
Retention time of xanomeline:12.2 min
Retention time of (LY246708 tartrate):14.5 min</td><td>[33]</td></tr>
</table>

	phosphorus detection			

Conclusion:

A wide range of analytical methods have been reported for the estimation of paliperidone, dexmedetomidine, and xanomeline, reflecting their clinical and pharmaceutical importance. Techniques such as UV spectrophotometry, HPLC, UPLC, GC, and LC–MS/MS have been successfully employed across different matrices, from bulk drug and formulations to biological fluids. Among these, HPLC and LC–MS/MS are most prominent, offering high sensitivity, selectivity, and reproducibility, making them ideal for pharmacokinetic, bioequivalence, and therapeutic monitoring studies. Meanwhile, spectrophotometric methods remain useful for routine quality control due to their simplicity and cost-effectiveness.

Acknowledgement:

The authors wish to express their sincere gratitude to the Department of Pharmaceutical sciences, Babasaheb Bhimrao Ambedkar University, for providing the necessary facilities and continuous support for the successful completion of this review.

Reference:

[1] P. Preet, R. Mishra, and B. Sharma, “A Review: Novel Analytical Method Development and Method Validation,” vol. 5, no. 8, **(2024),** pp. 32199–32208.

[2] M. Patel, D. Patel, K. Ahir, S. Singh, and S. S. A, “A Review: Development and validation of HPLC method Citation,” J Pharm Sci Bioscientific Res. 2019, vol. 9, no. 3, **(2019),** pp. 173–182.

[3] Suyash Gupta, Preeti Verma, Abhinav Prasoon Mishra, Nainshi Omar, and Riya Mathur, “A Review on Novel Analytical Method Development and Validation by RP-HPLC Method,” Indian Journal of Forensic Medicine & Toxicology, vol. 15, no. 4, **(2021),** pp. 3479–3486.

[4] G.A. Ugale, R.D. Chakole, M.S. Charde," UPLC in Pharmaceutical analysis", International Journal of Pharmacy and Pharmaceutical Research, vol. 24, no. 4, **(2022),** pp. 50-63.

[5] Vamsi Sai Krishna Kumar,” The Role of Mass Spectrometry in Modern Bioanalytical Method of Development”, International Journal of Pharmacy and Pharmaceutical Research, vol. 30, no. 7, **(2024)**, pp.149-164.

[6] S. Narwade, H. Wadkar, A. Ghanawat, and K. Nilwani, “A Comprehensive Review on HPTLC Method Development,” International Journal of Research and Review, vol. 12, no. 2, **(2025),** pp. 71–83.

[7] Pragya Nand Badyal, Chetan Sharma, Navdeep Kaur, Ravi Shankar, Abhay Pandey & Ravindra K. Rawal "Analytical Techniques in Simultaneous Estimation: An Overview", vol. 2, no. 2, **(2015)**, pp. 1037.

[8] K. P. Shinde and A. D. Rajmane, "A Review UV Method Development and Validation," Asian Journal of Pharmaceutical Analysis, vol. 13, no. 2, **(2023),** pp. 122–130.

[9] Vanitha Madhuri T, Santhosh Kumar Sorapalli, Kishore Babu Kagitha, "A Review of Liquid Chromatography -Mass Spectrometry and its applications in chemical analysis", vol. 2, no. 6, (2024), pp. 25-32.

[10] G. Schoretsanitis, E. Spina, C. Hiemke, and J. de Leon, "A systematic review and combined analysis of therapeutic drug monitoring studies for oral paliperidone," vol.11, no. 6, **(2018),** pp. 625-639.

[11] S. A. Jadhav, S. B. Landge, P. M. Choudhari, P. V. Solanki, S. R. Bembalkar, and V. T. Mathad, "Stress Degradation Behavior of Paliperidone, an Antipsychotic Drug, and Development of a Suitable Stability-Indicating RP-LC Method," Chromatography Research International, vol. 11, no. 6, **(2018),** pp. 625-639.

[12] F. Barbosa, L. Mantovani, C. V. Garcia, and A. S. L. Mendez, "Studies on Paliperidone in OROS Tablets: Extraction Procedure and Chromatographic Analysis," ISRN Chromatography, vol. 2012, Article ID 582375, **(2012)**, pp. 1–9

[13] M. A. S. Weerink, M. M. R. F. Struys, L. N. Hannivoort, C. R. M. Barends, A. R. Absalom, and P. Colin, "Clinical Pharmacokinetics and Pharmacodynamics of Dexmedetomidine," vol. 56, no. 8, **(2017),** pp. 893-913.

[14] S. Naaz and E. Ozair, "Dexmedetomidine in current anaesthesia practice- a review," Journal of Clinical and Diagnostic Research, vol. 8, no. 10, **(2014),** pp. GE01–GE04.

[15] M. K. O. Grant, M. J. Noetzel, K. C. De Lorme, J. Jakubík, V. Doležal, and E. E. El-Fakahany, "Pharmacological evaluation of the long-term effects of xanomeline on the M1 muscarinic acetylcholine receptor," PLoS One, vol. 5, no. 12, **(2010),** pp. E15722.

[16] A. M. Bender, C. K. Jones, and C. W. Lindsley, "Classics in Chemical Neuroscience: Xanomeline," vol.8, no. 3, **(2017)**, pp 435-443.

[17] J. Mathew, J. Chintankumar, and A. Jonils, "Analytical Method for the Estimation of Paliperidone", Vol. 2, no.2, **(2011),** pp.158-161

[18] R. K. Trivedi, P. Jain, M. C. Patel, P. M. Chatrabhuji, and D. R. Trivedi, "A rapid, stability indicating RP-UPLC method for determination of paliperidone palmitate in a depot injectable formulation," J Appl Pharm Sci, vol. 3, no. 7, **(2013),** pp. 87–92.

[19] M. P. Khanapure, D. S, B., N. Kalyani, and K. Hotkar, "UV Spectrophotometric Method for Estimation of Paliperidone in bulk and their solid dosage form," Asian Journal of Research in Chemistry and Pharmaceutical Sciences, vol. 08, no. 01, **(2020),** pp.78–83.

[20] M. C. Damle Professor, "Development and Validation of Stability Indicating HPTLC Method for Determination of Paliperidone Palmitate as Bulk Drug," JETIR, vol. 5, no. 8, **(2018),** pp. 309-316.

[21] R. B. Patel, M. R. Patel, K. K. Bhatt, and B. G. Patel, "HPTLC method development and validation: Quantification of paliperidone in formulations and in vitro release study," Analytical Methods, vol. 2, no. 5, **(2010),** pp. 525–531.

[22] S. Suman Panda, S. Beg, K. Ravi, V. Varaha, S. Priyadarshini Analytical, and J. Bioanal Biomed, "Quality-By-Design Compliant Ultrafast Liquid Chromatographic Method for Determination of Paliperidone in Extended-Release Tablet Dosage Form," J Bioanal Biomed, vol. 7, no. 4, **(2015),** pp. 4.

[23] F. Barbosa, L. Mantovani, C. V. Garcia, and A. S. L. Mendez, "Studies on Paliperidone in OROS Tablets: Extraction Procedure and Chromatographic Analysis," ISRN Chromatography, vol. 2012, no. 1, **(2012),** pp. 1–9.

[24] K. H. Bindu, N. H. Dhekale, M. V. Suryanarayana, and Y. Anjaneyulu, "A validated stability indicating UPLC method for simultaneous determination of assay, related substances, and degradation products of paliperidone palmitate active pharmaceutical ingredient and its pharmaceutical injection forms," J Liq Chromatogr Relat Technol, vol. 35, no. 4, **(2012),** pp. 533–546.

[25] N. Oza and S. Mali, "Development and validation of UV Spectroscopic method of paliperidone palmitate in bulk and its application for drug loading and entrapment efficiency analysis of long-acting injectable microspheres," International Journal of Applied Pharmaceutics, vol. 13, no. 4, **(2021),** pp. 87–93.

[26] R. Harika and S. Shobha Rani, "International Journal of Research Publication and Reviews Analytical Method Development and Validation for Dexmedetomidine HCL Injection by HPLC,"vol. 4, no. 12, **(2023),** pp. 1794-1800.

[27] K. P. Roopa, K. Basavaiah, and B. K. Jayanna, "Optimization and Validation of the Spectrophotometric Methods for the Assay of Dexmedetomidine Hydrochloride in Pure and Dosage Forms," J Appl Spectrosc, vol. 86, no. 4, **(2019),** pp. 740–747.

[28] M. Krishna, M. Nadre, A. Sherikar, and R. Reddy, "Stability Indicating HPLC Method Validation for the Assay of Dexmedetomidine in Dexmedetomidine Hydrochloride Injection" vol. 3, no.1, **(2015),** pp. 1-9.

[29] A. T. Murphy, P. L. Bonate, S. C. Kasper, T. A. Gillespie, and A. F. Delong, "Determination of Xanomeline in Human Plasma by Ionspray Tandem Mass Spectrometry," vol. 23, no. 10, **(1994),** pp. 621-625.

[30] S. C. Kasper, P. L. Bonate, and A. F. Delong, "High-performance liquid chromatographic assay for xanomeline, a specific M-1 agonist, and its metabolite in human plasma," vol. 669, no. 2, **(1995),** pp. 397-403.

[31] A. T. Murphy, S. C. Kasper, T. A. Gillespie, and A. F. Delong, "Determination of xanomeline and active metabolite, N-desmethylxanomeline, in human plasma by liquid chromatography-atmospheric pressure chemical ionization mass spectrometry," vol. 668, no. 2, **(1995),** pp. 273-280.

[32] P. Laxmiprasanna, R. S. Chandan, H. R. Nagidi, and N. Vidiyala, "Analytical Method Development and Validation of a Novel RP-HPLC Method for Simultaneous Quantification of Xanomeline and Trospium Chloride in Pharmaceutical Dosage Form," International Journal of Drug Delivery Technology, vol. 15, no. 1, **(2025),** pp. 119–125.

[33] T. J. Brown and L. A. Shipley, "Determination of xanomeline (LY246708 tartrate), an investigational agent for the treatment of Alzheimer's disease, in rat and monkey plasma by capillary gas chromatography with nitrogen-phosphorus detection," elsevier, vol. 665, no. 2, **(1995),** pp. 337-344.