



**IJPPR**

INTERNATIONAL JOURNAL OF PHARMACY & PHARMACEUTICAL RESEARCH  
An official Publication of Human Journals

ISSN 2349-7203




Human Journals

**Review Article**


July 2024 Vol.:30, Issue:7

© All rights are reserved by Vamsi sai Krishna Kumar

## Review Article: The Role of Mass Spectrometry in Modern Bioanalytical Method Development



**IJPPR**  
INTERNATIONAL JOURNAL OF PHARMACY & PHARMACEUTICAL RESEARCH  
An official Publication of Human Journals



ISSN 2349-7203

**Vamsi sai Krishna Kumar**

*Department of Pharmacy, Osmania University Main Road, Amberpet, Hyderabad 500007, India*

**Submitted:** 20 June 2024  
**Accepted:** 27 June 2024  
**Published:** 30 July 2024

**Keywords:** Mass spectrometry, bioanalytical methods, drug development, proteomics, metabolomics, clinical diagnostics, method validation, LC-MS, GC-MS.

### ABSTRACT

Mass spectrometry (MS) has revolutionized bioanalytical method development, providing unparalleled sensitivity, specificity, and versatility. This review highlights the critical role of MS in modern bioanalytical techniques, focusing on its application in drug development, proteomics, metabolomics, and clinical diagnostics. We discuss advancements in MS technology, the integration with chromatographic methods, and the regulatory considerations for method validation. Through various case studies, we illustrate how MS-based methods have enhanced biomolecule detection, quantification, and characterisation, ultimately driving innovation in biomedical research and pharmaceutical development.



HUMAN JOURNALS

[ijppr.humanjournals.com](http://ijppr.humanjournals.com)

## INTRODUCTION

Mass spectrometry (MS) is a powerful analytical technique used to measure the mass-to-charge ratio of ions. It is widely employed in various fields, including chemistry, biology, pharmacology, and environmental science because it provides detailed molecular information with high sensitivity and specificity. The technique has become indispensable in modern analytical laboratories for identifying, quantifying, and structuralising complex biological and chemical samples. [1-9]

### Basic Principles of Mass Spectrometry

Mass spectrometry's core principle involves ionising chemical compounds to generate charged molecules or molecule fragments and measuring their mass-to-charge ratios. A typical mass spectrometer consists of three main components:[10-17]

- **Ion Source:** This component ionises the sample molecules, converting them into charged particles (ions). Common ionisation techniques include Electrospray Ionization (ESI), Matrix-Assisted Laser Desorption/Ionization (MALDI), and Electron Impact Ionization (EI).
- **Mass Analyzer:** Once ionised, the ions are separated based on their mass-to-charge ratios. Different mass analysers are used, including quadrupole, time-of-flight (TOF), and Orbitrap analysers, each offering varying degrees of resolution and accuracy.
- **Detector:** The separated ions are detected, and their abundance is measured. The detector converts the ions' arrival into an electronic signal that can be recorded and analysed.

### Evolution of Mass Spectrometry

Since its inception, mass spectrometry (MS) has evolved remarkably, transitioning from basic instrumentation to sophisticated systems capable of high-resolution and high-throughput analyses. This evolution has significantly expanded MS's applications in various scientific fields. Here, we outline the key milestones and technological advancements that have shaped the development of MS. [18-22]

## Early Development and Foundations

Discovery and Early Instrumentation (Late 19th - Early 20th Century):

- **J.J. Thomson's Work:** In 1897, J.J. Thomson discovered the electron and developed the first mass spectrometer, which he used to measure the mass-to-charge ratio of ions. This work laid the foundation for mass spectrometry.
- **Aston's Mass Spectrograph:** In the 1910s, Francis W. Aston developed the mass spectrograph, which improved the resolution and allowed the identification of isotopes, earning him the Nobel Prize in Chemistry in 1922. [23-25]

#### Development of Sector Instruments (1930s - 1940s):

- **Double-Focusing Mass Spectrometers:** Instruments combining electric and magnetic fields were developed to improve mass resolution and accuracy. These early sector instruments were crucial in advancing isotopic and elemental analysis.[26,27]

#### Advancements in Ionization Techniques

##### 1. Electron Impact Ionization (EI) (1950s):

- **Widespread Use:** EI became the standard ionisation technique for many organic compounds, facilitating the development of mass spectral libraries and the identification of unknown compounds. [28,29]

##### 2. Chemical Ionization (CI) (1960s):

- **Soft Ionization:** CI provided a gentler ionisation method than EI, allowing the analysis of larger and more fragile molecules without extensive fragmentation. [30,31]

##### 3. Electrospray Ionization (ESI) and Matrix-Assisted Laser Desorption/Ionization (MALDI) (1980s - 1990s):

- **Revolutionizing Biomolecule Analysis:** ESI and MALDI enabled the ionisation of large biomolecules such as proteins and nucleic acids. These techniques have been pivotal in the fields of proteomics and genomics. [32,33]

#### High-resolution and High-Accuracy Mass Analyzers

##### 1. Time-of-Flight (TOF) Analyzers (1950s - 1960s):

- Speed and Sensitivity: TOF analysers offered rapid analysis and high sensitivity, making them suitable for high-throughput applications. [34,35]

#### 2. Quadrupole Mass Analyzers (1960s):

- Versatility and Affordability: Quadrupole analysers provided a balance between resolution, sensitivity, and cost, becoming widely used in routine analytical applications.

#### 3. Fourier Transform Ion Cyclotron Resonance (FT-ICR) (1970s - 1980s):

- Ultra-High Resolution: FT-ICR MS provided unprecedented resolution and mass accuracy, crucial for complex mixture analysis and identifying closely related molecular species.

#### 4. Orbitrap Analyzers (2000s):

- High Resolution and Accuracy: Orbitrap technology combined high resolution and mass accuracy with robust performance, enhancing the capabilities of high-resolution mass spectrometry (HRMS).

#### Hybrid Instruments and Coupled Techniques[38-45]

##### 1. LC-MS and GC-MS (1980s - 1990s):

- Separation and Analysis: The coupling of liquid chromatography (LC) and gas chromatography (GC) with MS provided powerful tools for the separation and analysis of complex mixtures. These hybrid techniques have become standard in many analytical laboratories.

##### 2. Tandem Mass Spectrometry (MS/MS) (1980s - 1990s):

- Structural Elucidation: MS/MS allowed for the sequential fragmentation of ions, providing detailed structural information and enhancing the identification and quantification of analytes.

#### Technological Innovations and Modern Developments

##### 1. Advances in Detector Technology:

- **Improved Sensitivity and Dynamic Range:** Innovations in detector design, such as electron multipliers and photomultiplier tubes, have enhanced the sensitivity and dynamic range of MS instruments.

## 2. Data Processing and Bioinformatics:

- **Enhanced Data Analysis:** The development of advanced data processing algorithms and bioinformatics tools has improved the interpretation of complex MS data, facilitating applications in systems biology and personalized medicine.

## 3. Miniaturization and Portable MS:

- **Field Applications:** The miniaturization of MS instruments has led to the development of portable MS devices, enabling on-site analysis in environmental monitoring, forensics, and clinical diagnostics.

### **Importance of Mass Spectrometry in Bioanalytical Techniques**

Mass spectrometry (MS) has become an essential tool in bioanalytical techniques due to its ability to provide precise, detailed, and reliable data on the molecular composition of complex biological samples. Here are some key reasons highlighting the importance of MS in bioanalytical methods:[46-57]

#### 1. High Sensitivity and Specificity

- **Detection of Low Abundance Compounds:** MS can detect and quantify compounds present in minute concentrations, which is crucial for studying low-abundance biomolecules such as hormones, vitamins, and trace metabolites.
- **Specificity in Identification:** The ability of MS to provide exact mass measurements and detailed fragmentation patterns allows for the specific identification of compounds, even in complex biological matrices.

#### 2. Comprehensive Analysis

- **Proteomics:** MS is indispensable in proteomics for identifying and quantifying proteins, characterizing post-translational modifications, and studying protein-protein interactions. Techniques like tandem mass spectrometry (MS/MS) allow for in-depth protein analysis.

- **Metabolomics:** In metabolomics, MS enables the comprehensive profiling of metabolites, providing insights into metabolic pathways, disease mechanisms, and biomarker discovery.
- **Lipidomics and Glycomics:** MS is also critical in lipidomics and glycomics for analyzing the complex structures and functions of lipids and glycans in biological systems.

### 3. Versatility and Flexibility

- **Broad Range of Applications:** MS can analyze a wide variety of biomolecules, including nucleic acids, proteins, lipids, and small molecules. This versatility makes it a fundamental tool in numerous research areas.
- **Coupling with Chromatographic Techniques:** The integration of MS with liquid chromatography (LC-MS) and gas chromatography (GC-MS) enhances its ability to separate, identify, and quantify components in complex mixtures, improving the analysis of biofluids, tissues, and other biological samples.

### 4. Quantitative and Qualitative Analysis

- **Accurate Quantification:** MS provides precise quantitative data on the concentration of analytes, which is essential for pharmacokinetic and pharmacodynamic studies, therapeutic drug monitoring, and clinical diagnostics.
- **Structural Elucidation:** MS can determine the molecular structure of unknown compounds through detailed mass spectra and fragmentation patterns, aiding in the identification of novel biomarkers and therapeutic targets.

### 5. High Throughput and Automation

- **Rapid Analysis:** Modern MS systems offer high-throughput capabilities, allowing for the rapid analysis of numerous samples. This is particularly valuable in large-scale studies such as clinical trials and population-based research.
- **Automation:** Advances in MS technology have led to the development of automated systems, which reduce manual intervention and improve reproducibility and accuracy in bioanalytical assays.

## 6. Regulatory Compliance and Validation

- **Method Validation:** MS methods can be validated according to regulatory guidelines (e.g., FDA, EMA), ensuring they meet the required standards for accuracy, precision, specificity, sensitivity, and robustness. This is crucial for their application in drug development, clinical diagnostics, and quality control.

## 7. Real-Time and In Vivo Analysis

- **Real-Time Monitoring:** MS techniques can be adapted to monitor biochemical processes and metabolic changes in real time, providing immediate data for dynamic studies.
- **In Vivo Applications:** The development of portable and miniaturised MS devices has enabled in vivo analysis, allowing for the direct measurement of compounds in living organisms, which is valuable for clinical diagnostics and environmental monitoring.

## **Applications in Bioanalytical Method Development**

Mass spectrometry (MS) has many applications in bioanalytical method development due to its exceptional sensitivity, specificity, and versatility. Here, we explore some of the key applications:[58-72]

### 1. Drug Development

- **Pharmacokinetics and Pharmacodynamics:** MS is critical for studying drug absorption, distribution, metabolism, and excretion (ADME). It helps determine the pharmacokinetic and pharmacodynamic profiles of new drugs by accurately quantifying drug concentrations in biological samples.
- **Metabolite Identification:** MS aids in identifying and characterising drug metabolites, ensuring that potential toxic metabolites are detected early in the drug development process.
- **Bioavailability and Bioequivalence Studies:** MS compares the bioavailability of different drug formulations, ensuring consistent therapeutic effects and regulatory compliance.

## 2. Proteomics

- **Protein Identification and Quantification:** MS-based proteomics allows for the comprehensive analysis of protein expression levels in various biological samples, aiding in identifying disease biomarkers and therapeutic targets.
- **Post-Translational Modifications (PTMs):** MS can detect and characterize PTMs, such as phosphorylation, glycosylation, and ubiquitination, providing insights into protein function and regulation.
- **Protein-Protein Interactions:** MS helps in studying protein complexes and interactions, which are crucial for understanding cellular processes and signaling pathways.

## 3. Metabolomics

- **Metabolic Profiling:** MS enables the analysis of small molecules and metabolites in biological samples, providing insights into metabolic pathways and their alterations in diseases.
- **Biomarker Discovery:** By identifying changes in metabolite concentrations, MS helps discover biomarkers for early disease detection, prognosis, and therapeutic monitoring.
- **Nutritional and Environmental Studies:** MS is used to study the effects of diet, lifestyle, and environmental factors on metabolism, contributing to personalized medicine and public health.

## 4. Clinical Diagnostics

- **Disease Diagnosis:** MS-based assays are used to detect specific biomarkers for various diseases, including cancer, cardiovascular diseases, and metabolic disorders. These assays offer high sensitivity and specificity, enabling early and accurate diagnosis.
- **Therapeutic Drug Monitoring:** MS quantifies drug levels in patients' blood, ensuring they remain within the therapeutic range, optimizing treatment efficacy and minimizing side effects.
- **Newborn Screening:** MS is employed in screening newborns for metabolic and genetic disorders, enabling early intervention and improved outcomes.



## 5. Environmental and Food Safety

- **Contaminant Detection:** MS is used to detect and quantify environmental pollutants, pesticides, and other contaminants in air, water, and soil samples, ensuring compliance with safety regulations.
- **Food Quality Control:** MS helps in identifying and quantifying food additives, contaminants, and adulterants, ensuring food safety and quality.

## 6. Forensic Analysis

- **Toxicology:** MS is used in forensic toxicology to detect and quantify drugs, poisons, and other toxic substances in biological samples, aiding in criminal investigations and legal proceedings.
- **Drug Testing:** MS-based methods are used for doping control in sports and workplace drug testing, offering high sensitivity and specificity.

## 7. Systems Biology

- **Comprehensive Omics Analysis:** MS integrates data from genomics, proteomics, and metabolomics, providing a holistic view of biological systems and their functions.
- **Pathway Analysis:** MS helps in mapping metabolic and signaling pathways, understanding their roles in health and disease.

## 8. Personalized Medicine

- **Theranostics:** MS aids in developing theranostic approaches, which combine diagnostics with therapeutics to tailor treatments based on individual patient profiles.
- **Pharmacogenomics:** MS helps in studying the impact of genetic variations on drug response, contributing to personalized drug therapy.

## Integration with Chromatographic Methods

The coupling of MS with chromatographic techniques such as LC and GC has transformed bioanalytical methods by improving the separation and quantification of analytes in complex

matrices. LC-MS and GC-MS are standard laboratory tools, offering enhanced sensitivity and specificity.

### **Regulatory Considerations**

Method validation is crucial for ensuring the reliability and reproducibility of MS-based bioanalytical methods. Regulatory guidelines, such as those from the U.S. Food and Drug Administration (FDA) and the European Medicines Agency (EMA), outline the requirements for accuracy, precision, specificity, sensitivity, and stability. Adhering to these guidelines is essential for accepting MS methods in clinical and pharmaceutical applications.[73-93]

### **Case Studies**

1. **Quantification of BioTherapeutics:** MS quantifies monoclonal antibodies and other biotherapeutics in biological matrices, demonstrating its utility in pharmacokinetic studies.
2. **Biomarker Discovery in Cancer:** MS-based proteomics has identified potential biomarkers for early cancer detection, providing a foundation for developing diagnostic assays.
3. **Metabolic Profiling in Diabetes:** MS metabolomics has elucidated metabolic alterations in diabetic patients, contributing to understanding disease progression and treatment efficacy.

### **Conclusion**

Mass spectrometry continues to advance bioanalytical method development, offering robust, sensitive, and specific analytical capabilities. Its integration with chromatographic techniques and adherence to regulatory standards ensure its continued relevance in drug development, proteomics, metabolomics, and clinical diagnostics. As MS technology evolves, it will undoubtedly drive further innovations in bioanalytical science, enhancing our ability to study and understand complex biological systems.

### **References**

1. Reddy KT, Haque MA. Develop and validate a highly sensitive method for estimating Molnupiravir in rat plasma by high-performance liquid chromatography-tandem mass spectroscopy and its application to pharmacokinetic studies. *Journal of Pharmaceutical Negative Results*. 2022 Sep 21:28-34.
2. Gandla K, Reddy KT, Babu PV, Sagapola R, Sudhakar P. A review of artificial intelligence in treatment of COVID-19. *Journal of Pharmaceutical Negative Results*. 2022 Sep 15:254-64.
3. Reddy KT, Haque MA. Bioanalytical method development and validation of atrasentan in human plasma using verapamil as internal standard by liquid chromatography coupled with tandem mass spectrometry. *International Journal of Health Sciences*. 2022;6:625-38.

4. Reddy KT, Haque MA. Development and Validation of a High Throughput Lc-MS/MS Method for Quantitation of Ipilimumab in Human Plasma. *International Journal of Pharmaceutical Quality Assurance*. 2022;13(3):303-7.
5. Konatham TK. A Systematic Review on Method Development and Validation of Few Antiviral Drugs Using RP-HPLC. *Ijpr. Human*. 2021;21(3):651-61.
6. Reddy KTK, Haque MA. Molnupiravir Bioanalytical Method Development and Validation in Rat Plasma by LC-MS/MS Detection and Application to a Pharmacokinetic Study. *International Journal of Pharmaceutical Quality Assurance*. 2024;15(1):110-114.
7. Reddy KTK, Haque MA. LC-MS/MS Bioanalytical Procedure for Atrasentan in Human Plasma: Method Development and Validation. *International Journal of Pharmaceutical Quality Assurance*. 2024;15(2):605-610
8. Papinaboina Venkata Rao, Chinnakadoori Sanjeeva Reddy, Ravi Kumar Marram, Dantu Durga Rao, Simultaneous Determination Of Omeprazole And Domperidone In Capsules And *In Vitro* Dissolution Studies By Using Stability Indicating UPLC, *Journal of liquid chromatography & related technologies*, 2012, 35 (16), 2322-2332. <https://doi.org/10.1080/10826076.2011.631262>.
9. Niroja Vadagam, Sharath Babu Haridasyam, Muvvala Venkatanarayana, Narasimha S. Lakka, Sanjeeva R. Chinnakadoori, Separation and quantitative estimation of stereo-selective enantiomers of montelukast in pharmaceutical drug substance and tablets dosage forms by using stability-indicating normal phase-HPLC method, *Chirality*, 2023, 35(12), 952-965. <https://doi.org/10.1002/chir.23610>.
10. Niroja Vadagam, Sharath Babu Haridasyam, Muvvala Venkatanarayana, Narasimha S Lakka, Sanjeeva R Chinnakadoori, Separation and quantitation of valacyclovir enantiomers using stability-indicating chiral liquid chromatography method with a chiral stationary phase of amylose tris-(3,5-dimethylphenylcarbamate), *Separation Science Plus*, 2023, 6(12), 2300145. <https://doi.org/10.1002/sscp.202300145>
11. Narasimha S Lakka, Chandrasekar Kuppan, Niroja Vadagam, Poornima Ravinathan, Kalyani Chepuri, Sanjeeva R Chinnakadoori, Molecular docking, in-vitro anticancer evaluation and ADME profiling of 7-Oxo Midostaurin, *Journal of Molecular Structure*, 2023, 1293, 136159. <https://doi.org/10.1016/j.molstruc.2023.136159>
12. Niroja Vadagam, Sharath Babu Haridasyam, Muvvala Venkatanarayana, Narasimha S Lakka, Sanjeeva R Chinnakadoori, Separation and simultaneous estimation of enantiomers and Diastereomers of muscarinic receptor antagonist Solifenacin using stability-indicating Normal-phase HPLC technique with chiral stationary phase amylose tris-(3,5-dimethylphenylcarbamate), *Chirality*, 2024, 36(2), e23632. <https://doi.org/10.1002/chir.23632>
13. Mohan Pasham, Sharath Babu Haridasyam, Niroja Vadagam, NVVD Praveen Boppy, Sanjeeva R Chinnakadoori, Narasimha S Lakka, Separation and quantification of organic-related impurities of beta-adrenergic receptor blocking agent propranolol in pharmaceutical solid dosage forms: Impurity profiling using stability-indicating HPLC method, 2024, 7(1), 2300159. <https://doi.org/10.1002/sscp.202300159>
14. N. V. V. D. Praveen Boppy, Sharath Babu Haridasyam, Niroja Vadagam, Muvvala Venkatanarayana, Sanjeeva R. Chinnakadoori, Narasimha S. Lakka, Separation and quantification of organic-related impurities of anti-histamine drug hydroxyzine in pharmaceutical dosage forms using stability-indicating high-performance liquid chromatography, liquid chromatography-mass spectrometry, and high-resolution mass spectrometry techniques, *Separation Science Plus*, 2024, 2300157. <https://doi.org/10.1002/sscp.202300157>
15. Yelampalli SR, Gandla K, Reddy KT, Ibrahim AE, El Deeb S. Determination of sodium, potassium, and magnesium as sulfate salts in oral preparations using ion chromatography and conductivity detection. *Separations*. 2023 Feb 1;10(2):99.
16. Teja MS, Konatham TR, Muralidharan V, Murugesan A, Vasantha N, Hyandavi M. A Review on Biosensors for Covid-19. *International Journal of Applied Pharmaceutical Sciences And Research*. 2022 Jan 1;7(01):9-14.
17. Baig MS, Haque MA, Konatham TK, Mohammad BD, Yahya BA, Saffiruddin SS, Siddiqui FA, Khan SL. Recent Advancements in Hyperthermia-Driven Controlled Drug Delivery from Nanotherapeutics. *Recent Advances in Drug Delivery and Formulation: Formerly Recent Patents on Drug Delivery & Formulation*. 2022 Dec 1;16(4):270-86.
18. Reddy KT, Venkatesan N, Saranya MV, Somasundaram J, Gupta JK, Priya NS, Sukhramani PS, Patil A. Cytotoxicity of Quantum Dots Based Nanocomposites. In *Quantum Dots Based Nanocomposites: Design, Fabrication and Emerging Applications* 2024 Jun 2 (pp. 207-229).

19. Reddy KT, Venkata Badarinath A, Gupta JK, Manikanta Y, Priya NS, Vamseekrishna G, Alex J, Sahithi A. Synthesis Strategies of Doped QDs. In Quantum Dots Based Nanocomposites: Design, Fabrication and Emerging Applications 2024 Jun 2 (pp. 35-62).
20. Reddy KT, Madhavi Latha B, Gupta JK, Chaitanya A, Srinivasa Babu P, Manikanta Y, Sahithi A. Discovery and History of Quantum Dots. In Quantum Dots Based Nanocomposites: Design, Fabrication and Emerging Applications 2024 Jun 2 (pp. 13-34).
21. Reddy KT, Haque MA. Develop and validate a highly sensitive method for estimating Molnupiravir in rat plasma by high-performance liquid chromatography-tandem mass spectroscopy and its application to pharmacokinetic studies. Journal of Pharmaceutical Negative Results. 2022 Sep 21:28-34.
22. Gandla K, Reddy KT, Babu PV, Sagapola R, Sudhakar P. A review of artificial intelligence in treatment of COVID-19. Journal of Pharmaceutical Negative Results. 2022 Sep 15:254-64.
23. Reddy KT, Haque MA. Bioanalytical method development and validation of atrasentan in human plasma using verapamil as internal standard by liquid chromatography coupled with tandem mass spectrometry. International Journal of Health Sciences. 2022;6:625-38.
24. Reddy KT, Haque MA. Development and Validation of a High Throughput Lc-MS/MS Method for Quantitation of Ipilimumab in Human Plasma. International Journal of Pharmaceutical Quality Assurance. 2022;13(3):303-7.
25. Konatham TK. A Systematic Review on Method Development and Validation of Few Antiviral Drugs Using RP-HPLC. Ijppr. Human. 2021;21(3):651-61.
26. Reddy KTK, Haque MA. Molnupiravir Bioanalytical Method Development and Validation in Rat Plasma by LC-MS/MS Detection and Application to a Pharmacokinetic Study. International Journal of Pharmaceutical Quality Assurance. 2024;15(1):110-114.
27. Reddy KTK, Haque MA. LC-MS/MS Bioanalytical Procedure for Atrasentan in Human Plasma: Method Development and Validation. International Journal of Pharmaceutical Quality Assurance. 2024;15(2):605-610
28. Papinaboina Venkata Rao, Chinnakadoori Sanjeeva Reddy, Ravi Kumar Marram, Dantu Durga Rao, Simultaneous Determination Of Omeprazole And Domperidone In Capsules And *In Vitro* Dissolution Studies By Using Stability Indicating UPLC, Journal of liquid chromatography & related technologies, 2012, 35 (16), 2322-2332. <https://doi.org/10.1080/10826076.2011.631262>.
29. Niroja Vadagam, Sharath Babu Haridasyam, Muvvala Venkatanarayana, Narasimha S. Lakka, Sanjeeva R. Chinnakadoori, Separation and quantitative estimation of stereo-selective enantiomers of montelukast in pharmaceutical drug substance and tablets dosage forms by using stability-indicating normal phase-HPLC method, Chirality, 2023, 35(12), 952-965. <https://doi.org/10.1002/chir.23610>.
30. Niroja Vadagam, Sharath Babu Haridasyam, Muvvala Venkatanarayana, Narasimha S Lakka, Sanjeeva R Chinnakadoori, Separation and quantitation of valacyclovir enantiomers using stability-indicating chiral liquid chromatography method with a chiral stationary phase of amylose tris-(3,5-dimethylphenylcarbamate), Separation Science Plus, 2023, 6(12), 2300145. <https://doi.org/10.1002/sscp.202300145>
31. Narasimha S Lakka, Chandrasekar Kuppan, Niroja Vadagam, Poornima Ravinathan, Kalyani Chepuri, Sanjeeva R Chinnakadoori, Molecular docking, in-vitro anticancer evaluation and ADME profiling of 7-Oxo Midostaurin, Journal of Molecular Structure, 2023, 1293, 136159. <https://doi.org/10.1016/j.molstruc.2023.136159>
32. Niroja Vadagam, Sharath Babu Haridasyam, Muvvala Venkatanarayana, Narasimha S Lakka, Sanjeeva R Chinnakadoori, Separation and simultaneous estimation of enantiomers and Diastereomers of muscarinic receptor antagonist Solifenacin using stability-indicating Normal-phase HPLC technique with chiral stationary phase amylose tris-(3,5-dimethylphenylcarbamate), Chirality, 2024, 36(2), e23632. <https://doi.org/10.1002/chir.23632>
33. Mohan Pasham, Sharath Babu Haridasyam, Niroja Vadagam, NVVD Praveen Boppy, Sanjeeva R Chinnakadoori, Narasimha S Lakka, Separation and quantification of organic-related impurities of beta-adrenergic receptor blocking agent propranolol in pharmaceutical solid dosage forms: Impurity profiling using stability-indicating HPLC method, 2024, 7(1), 2300159. <https://doi.org/10.1002/sscp.202300159>
34. N. V. V. D. Praveen Boppy, Sharath Babu Haridasyam, Niroja Vadagam, Muvvala Venkatanarayana, Sanjeeva R. Chinnakadoori, Narasimha S. Lakka, Separation and quantification of organic-related impurities of anti-histamine drug hydroxyzine in pharmaceutical dosage forms using stability-indicating

high-performance liquid chromatography, liquid chromatography-mass spectrometry, and high-resolution mass spectrometry techniques, *Separation Science Plus*, 2024, 2300157. <https://doi.org/10.1002/sscp.202300157>

35. Yelampalli SR, Gandla K, Reddy KT, Ibrahim AE, El Deeb S. Determination of sodium, potassium, and magnesium as sulfate salts in oral preparations using ion chromatography and conductivity detection. *Separations*. 2023 Feb 1;10(2):99.

36. Teja MS, Konatham TR, Muralidharan V, Murugesan A, Vasantha N, Hyandavi M. A Review on Biosensors for Covid-19. *International Journal of Applied Pharmaceutical Sciences And Research*. 2022 Jan 1;7(01):9-14.

37. Baig MS, Haque MA, Konatham TK, Mohammad BD, Yahya BA, Saffiruddin SS, Siddiqui FA, Khan SL. Recent Advancements in Hyperthermia-Driven Controlled Drug Delivery from Nanotherapeutics. *Recent Advances in Drug Delivery and Formulation: Formerly Recent Patents on Drug Delivery & Formulation*. 2022 Dec 1;16(4):270-86.

38. Reddy KT, Venkatesan N, Saranya MV, Somasundaram J, Gupta JK, Priya NS, Sukhramani PS, Patil A. Cytotoxicity of Quantum Dots Based Nanocomposites. In *Quantum Dots Based Nanocomposites: Design, Fabrication and Emerging Applications 2024 Jun 2* (pp. 207-229).

39. Reddy KT, Venkata Badarinath A, Gupta JK, Manikanta Y, Priya NS, Vamseekrishna G, Alex J, Sahithi A. Synthesis Strategies of Doped QDs. In *Quantum Dots Based Nanocomposites: Design, Fabrication and Emerging Applications 2024 Jun 2* (pp. 35-62).

40. Reddy KT, Madhavi Latha B, Gupta JK, Chaitanya A, Srinivasa Babu P, Manikanta Y, Sahithi A. Discovery and History of Quantum Dots. In *Quantum Dots Based Nanocomposites: Design, Fabrication and Emerging Applications 2024 Jun 2* (pp. 13-34).

41. Madhu Medabalimi, Saravanakumar Kasimedu, S.V. Satyanarayana, A Novel UPLC Method for the Estimation of Antidiabetic Drugs in Bulk and its Tablet dosage form, *Asian Journal of Pharmaceutics Oct-Dec 2023*; 17(4), 803-810. (IF 0.5)I: Thomson Reuters(Web of Science), Publon DOI: <https://doi.org/10.22377/ajp.v17i04>

42. Madhu Medabalimi, Saravanakumar Kasimedu, S.V. Satyanarayana, UPLC Method Development and Validation for The Simultaneous Estimation of Cytarabine and Daunorubicin in Pharmaceutical Dosage Form, *Journal of Pharmaceutical Negative Results 2022*; 13(07): 7816-7825. (IF 1.65) I: SCI & P: ResearchTrentz & Print -0976-9234, Online - 2229-7723 DOI: <https://www.pnrjournal.com/index.php/home/article/view/9520>

43. Jagadeesh Yelamanda, Saravanakumar K, Kavitha Mutharasi, Terbinafine hydrochloride emulgel – formulation development and characterization, *YMER 2022*; 21(11): 1903-1912. I: SCOPUS & P: Swedish Society for Anthropology and Geography & 0044-0477.DOI: <http://ymerdigital.com/archives/?cpage=8&issId=%202111>

44. Prudhvi Raj V, Saravanakumar K, Yugandhar Baiiah, Formulation Design and Characterization of Orally Disintegrating Tablet of Rizatriptan Using Different Superdisintegrants, *YMER 2022*; 21(11): 1181-1191. I: SCOPUS & P: Swedish Society for Anthropology and Geography & 0044-0477 I: SCOPUS & P: Swedish Society for Anthropology and Geography & 0044-0477 DOI: <http://ymerdigital.com/archives/?cpage=5&issId=%202111>

45. Swetha Arumilli, Saravanakumar K, Divya Sree M. S, Divya Rekha O, Formulation development and evaluation of polyherbal natural facepack for skin ailments, *YMER 2022*; 21(11): 683-693.: SCOPUS & P: Swedish Society for Anthropology and Geography & 0044-0477DOI: <http://ymerdigital.com/archives/?cpage=3&issId=%202111>

46. Madhu Medabalimi, Saravanakumar K\*, Satyanarayana S.V., Development and Validation of Stability Indicating RP-HPLC Method for Quantitative Estimation of Safinamide Mesylate in Bulk and its Tablet Dosage Form, *Current Trends in Biotechnology and Pharmacy*, 2022; 16(2): 50-59.I: WOS P: Association of Biotechnology and Pharmacy & 2230-7303DOI: <https://abap.co.in/index.php/home/article/view/603/184>

47. Saravanakumar Kasimbedu\*, Shilpaja Chella, Bharathi T, Nagaveni Pommala, Durga Srinivasa Rao Mannepalli, A Piroxicam Inclusion Complexation for Solubility Enhancement: Design and Development, *J Young Pharm*, 2022; 14(2) : 192-197. IF 0.542I: WOS & P: EMANUSCRIPT TECHNOLOGIES & P-ISSN - 0975-1483DOI: <https://dx.doi.org/10.5530/jyp.2022.14.36>

48. Durga Srinivasarao M, Saravanakumar K\*, Chandrasekhar Kothapalli Bannoth, Formulation Development and Characterization of Baclofen Floating Drug Delivery System, *Asian Journal of Pharmaceutics 2021*; 15(4):



- 452-458. IF 0.360I: WOS P: Medknow Publications & 0973-8398 (print) 1998-409X (web) DOI: <https://dx.doi.org/10.22377/ajp.v15i04.4227>
49. Saravanakumar K, Radhika C, Chandra Sekhar Kothapalli Bannoth, Pharmacological Screening of *Amaranthus roxburghianus* Nevski Total Flavonoids for Anti-Arthritic Activity in Freund's Complete Adjuvant-Induced Arthritis Rat Model, *Bioscience Biotechnology Research Communications* 2021, 14(2), 728-733. IF 3.322 I: Scopus P: Society for Science and Nature Bhopal India & 0974-6455 E-ISSN: 2321-4007 DOI: <http://dx.doi.org/10.21786/bbrc/14.2.44>
50. Durga Srinivasarao M, Saravanakumar K\*, Chandrasekhar Kothapalli Bannoth, Formulation Development and Characterization of Baclofen Floating Drug Delivery System, *Asian Journal of Pharmaceutics* 2021, 15(4), 448-452. IF 0.360 I: WOS P: Medknow Publications & 0973-8398 (print) 1998-409X (web) DOI: <http://dx.doi.org/10.22377/ajp.v15i04.4227>
51. Radhika Chikatipalli, Saravanakumar K, Chandra Sekhar Kothapalli Bannoth, Pharmacognostic evaluation and free radical scavenging activity of *Bombax ceiba* leaf extracts, *International Journal of Green Pharmacy* 2021, 15 (1), 59-65. IF 0.269I: SCOPUS P: Medknow Publications & P-ISSN - 0973-8258. E-ISSN - 1998-4103 DOI: <http://dx.doi.org/10.22377/ijgp.v15i1.3016>
52. Saravanakumar K\*, Durga Srinivasa Rao M, Kothapalli Bannoth Chandrasekhar, Combination Effect of Natural and Synthetic Polymers in Extending the Release of Tolperisone HCl from its Effervescent Floating Tablets, *Research J. Pharm. and Tech.* 2021, 14(1), 171-178. IF 0.267I: SCI P: A&V Publications & 09743618, 0974360X DOI: 10.5958/0974-360X.2021.00030.5.
53. Papinaboina Venkata Rao, Chinnakadoori Sanjeeva Reddy, Ravi Kumar Marram, Dantu Durga Rao, Simultaneous Determination Of Omeprazole And Domperidone In Capsules And *In Vitro* Dissolution Studies By Using Stability Indicating UPLC, *Journal of liquid chromatography & related technologies*, 2012, 35 (16), 2322-2332. <https://doi.org/10.1080/10826076.2011.631262>.
54. Niroja Vadagam, Sharath Babu Haridasyam, Muvvala Venkatanarayana, Narasimha S. Lakka, Sanjeeva R. Chinnakadoori, Separation and quantitative estimation of stereo-selective enantiomers of montelukast in pharmaceutical drug substance and tablets dosage forms by using stability-indicating normal phase-HPLC method, *Chirality*, 2023, 35(12), 952-965. <https://doi.org/10.1002/chir.23610>.
55. Niroja Vadagam, Sharath Babu Haridasyam, Muvvala Venkatanarayana, Narasimha S Lakka, Sanjeeva R Chinnakadoori, Separation and quantitation of valacyclovir enantiomers using stability-indicating chiral liquid chromatography method with a chiral stationary phase of amylose tris-(3,5-dimethylphenylcarbamate), *Separation Science Plus*, 2023, 6(12), 2300145. <https://doi.org/10.1002/sscp.202300145>
56. Narasimha S Lakka, Chandrasekar Kuppan, Niroja Vadagam, Poornima Ravinathan, Kalyani Chepuri, Sanjeeva R Chinnakadoori, Molecular docking, in-vitro anticancer evaluation and ADME profiling of 7-Oxo Midostaurin, *Journal of Molecular Structure*, 2023, 1293, 136159. <https://doi.org/10.1016/j.molstruc.2023.136159>
57. Niroja Vadagam, Sharath Babu Haridasyam, Muvvala Venkatanarayana, Narasimha S Lakka, Sanjeeva R Chinnakadoori, Separation and simultaneous estimation of enantiomers and Diastereomers of muscarinic receptor antagonist Solifenacin using stability-indicating Normal-phase HPLC technique with chiral stationary phase amylose tris-(3,5-dimethylphenylcarbamate), *Chirality*, 2024, 36(2), e23632. <https://doi.org/10.1002/chir.23632>
58. Mohan Pasham, Sharath Babu Haridasyam, Niroja Vadagam, NVVD Praveen Boppy, Sanjeeva R Chinnakadoori, Narasimha S Lakka, Separation and quantification of organic-related impurities of beta-adrenergic receptor blocking agent propranolol in pharmaceutical solid dosage forms: Impurity profiling using stability-indicating HPLC method, 2024, 7(1), 2300159. <https://doi.org/10.1002/sscp.202300159>
59. N. V. V. D. Praveen Boppy, Sharath Babu Haridasyam, Niroja Vadagam, Muvvala Venkatanarayana, Sanjeeva R. Chinnakadoori, Narasimha S. Lakka, Separation and quantification of organic-related impurities of anti-histamine drug hydroxyzine in pharmaceutical dosage forms using stability-indicating high-performance liquid chromatography, liquid chromatography-mass spectrometry, and high-resolution mass spectrometry techniques, *Separation Science Plus*, 2024, 2300157. <https://doi.org/10.1002/sscp.202300157>
60. Reddy KT, Haque MA. Develop and validate a highly sensitive method for estimating Molnupiravir in rat plasma by high-performance liquid chromatography-tandem mass spectroscopy and its application to pharmacokinetic studies. *Journal of Pharmaceutical Negative Results*. 2022 Sep 21:28-34.

61. Gandla K, Reddy KT, Babu PV, Sagapola R, Sudhakar P. A review of artificial intelligence in treatment of COVID-19. *Journal of Pharmaceutical Negative Results*. 2022 Sep 15:254-64.
62. Reddy KT, Haque MA. Bioanalytical method development and validation of atrasentan in human plasma using verapamil as internal standard by liquid chromatography coupled with tandem mass spectrometry. *International Journal of Health Sciences*. 2022;6:625-38.
63. Reddy KT, Haque MA. Development and Validation of a High Throughput Lc-MS/MS Method for Quantitation of Ipilimumab in Human Plasma. *International Journal of Pharmaceutical Quality Assurance*. 2022;13(3):303-7.
64. Konatham TK. A Systematic Review on Method Development and Validation of Few Antiviral Drugs Using RP-HPLC. *Ijppr. Human*. 2021;21(3):651-61.
65. Reddy KTK, Haque MA. Molnupiravir Bioanalytical Method Development and Validation in Rat Plasma by LC-MS/MS Detection and Application to a Pharmacokinetic Study. *International Journal of Pharmaceutical Quality Assurance*. 2024;15(1):110-114.
66. Reddy KTK, Haque MA. LC-MS/MS Bioanalytical Procedure for Atrasentan in Human Plasma: Method Development and Validation. *International Journal of Pharmaceutical Quality Assurance*. 2024;15(2):605-610
67. Saravanakumar K\*, Pommala Nagaveni, Dwarakanadha Reddy Peram, Formulation and Evaluation of Meloxicam pH Induced *In-situ* Gels, *Int. J. of Clin. Pharm. Med. Sci.* 2021; 1(1): 23-27. DOI: <https://pharmasprings.com/ijcpms/article/view/24>
68. Saravanakumar Kasimedu, Hemalatha Palavuri, Swathi Puchakayala, Dhanalakshmi Rayavarapu, Background, Trends, Applications and Therapeutic Approaches of Nanoparticles: A Review, *Future J. Pharm. Health. Sci.* 2023; 3(4): 461-470. DOI: <https://doi.org/10.26452/fjphs.v3i4.523>
69. Prudhvi Raj V, Jagadeesh Y, Saravanakumar K, Solid Lipid Nanoparticles: A Novel Method to Drug Delivery Formulation, *Int. J. Exp. Biomed. Res.* 2023; 2(1): 1-10. DOI: <https://doi.org/10.26452/ijebr.v2i1.441>
70. Saravanakumar K, Bhavani Guvvala, Shilpaja Chella, Prudhvi Raj Vadamala, Swamy Charan Dontha, Floating Drug Delivery Systems - Challenges & Approaches, *YMER* 2022; 21(11): 997-1009. DOI: <http://ymerdigital.com/archives/?cpage=5&issId=%202111>
71. Saravanakumar K, Swamy Charan Dontha, Shaik Afreen Taj Jataka, Alzheimers disease upon pathological hypothesis & the stages of disease - a review on its current and future, *YMER* 2022; 21(11): 868-878. DOI: <http://ymerdigital.com/archives/?cpage=4&issId=%202111>
72. Sreedhar V, Saravanakumar K, Sai Sri Harsha G, Subhasish Debnath, A Case Report On Anaphylactic Shock (INJ.IRON SUCROSE), *International Journal of Biology, Pharmacy and Allied Sciences*, 2022, 11(9), 4355-4360. DOI: <https://doi.org/10.31032/IJBPAS/2022/11.9.6420>
73. Durga Srinivasarao M, Saravanakumar K, ChandraSekhar Kothapalli Bannoth, Gastro-retentive drug delivery systems: a review with focus on floating drug delivery systems, *International Journal of Research in Pharmaceutical Sciences*, 2021, 12(2), 1330-1337.
74. Swathi Gadiraju, Sireesha Reddy Pilaka, Saravanakumar K, Photodynamic Therapy Combined With Nanocarriers for Breast Cancer Treatment: An Updated Review, *World Journal of Pharmacy and Pharmaceutical Science* 2021, 10(9), 2054-2072.
75. Saravanakumar K, Vani P, Ashok Kumar C K, Amulya J, Muni Taraknath LM, A Review on Self Micro Emulsifying Drug Delivery System. *Inventi Rapid: NDDS*, 2016 (3), 1-4.
76. Saravanakumar K, Poojitha K, Sanjeev Rao T, Vani P, Swapna P, Self Double Emulsifying Drug Delivery Sytem: A Review, *Inventi Rapid: Pharm Tech Vol.* 2015, Issue 4, 1-3.
77. Saravanakumar K, Sanjeev Rao T, Nagaveni P, A review on solubility enhancement techniques. *Journal of Comprehensive Pharmacy* 2015, 2(2), 36-41. URL: <http://doi.org/10.37483/JCP.2015.2202>
78. Saravanakumar K, Swapna P, Nagaveni P. Transdermal drug delivery system: A review. *Journal of Global Trends in Pharmaceutical Sciences* 2015, 6(1), 2485 – 2490.
79. Vidyavathi N, Anitha K, Saravanakumar K. *Bauhinia tomentosa*: A review. *Journal of Comprehensive Pharmacy* 2015, 2(1), 27-30. DOI URL: <http://doi.org/10.37483/JCP.2015.2105>
80. Poorna Theja K, Ramesh Y, Ashok kumar K, Saravanakumar K. A review on medicated chewing gums. *International Journal of Institutional Pharmacy and Life Sciences* 2015, 5(1), 124-136. URL: Microsoft Word - E Print IJIPLS 5 \_1\_-14-124-136 Pharmaceutical Sciences\_Research Article

81. Anitha K, Mohana Lakshmi S, Saravanakumar K. The potential role of herbals as nephroprotective – a novel approach. *Journal of Comprehensive Pharmacy* 2015, 2(1), 18-26. DOI URL: <http://doi.org/10.37483/JCP.2015.2104>
82. Vivek Kumar P, Saravanakumar K, Nagaveni P. A review on floating drug delivery systems. *International Journal of Research in Pharmaceutical Sciences* 2014, 5(3), 193-199.
83. Ramesh B, Saravanakumar K, Nagaveni P. A review on buccal drug delivery system. *International Journal of Research in Pharmaceutical Sciences* 2014, 5(3), 200-2004.
84. Mohan Kumar A, Saravanakumar K, Nagaveni P. Novel review on mucoadhesive drug delivery system. *International Journal of Research in Pharmaceutical Sciences* 2014, 5(3), 205-215.
85. Ramesh B, Saravanakumar K, Jagadish Kumar K. A novel approach of fast dissolving films: A review. *International Journal of Medicine and Pharmaceutical Research* 2014, 2(5), 740-748.
86. Sasi Deepthi K, Saravanakumar K, Mohana Lakshmi S. *Momordica charantia* in diabetic management: a mini review. *Journal of Global Trends in Pharmaceutical Sciences* 2014, 4(4), 1271-1278.
87. Vijay Kumar N, Saravanakumar K, Prasanna Raju Y. Nano-emulsion - A novel and emerging trend. *Inventi NDDS* 2013, 3, 1-5.
88. Saravanakumar K, Sushma M, Prasanna Raju Y. Dissolution enhancement of poorly soluble drugs by using complexation technique – A review. *Journal of Pharmaceutical Science & Research* 2013, 5(5), 120 - 124.
89. Saravanakumar K, Jayachandra Reddy P, Chandra Sekhar KB. A review on microsphere for novel drug delivery system. *Journal of Pharmacy Research* 2012, 5(1), 420-424.
90. Saravanakumar K, Jayachandra Reddy P, Chandra Sekhar KB. A review on management of myasthenia gravis. *International Journal of Research in Pharmaceutical Sciences* 2011, 2(4), 648-653.
91. Saravanakumar K, Jayachandra Reddy P, Chandra Sekhar KB. Polymers in mucoadhesive microsphere drug delivery system: A review. *Journal of Global Trends in Pharmaceutical Sciences* 2011, 2(3), 249-263.
92. Saravanakumar K, Nagaveni P, Chandra Sekhar KB, Jayachandra Reddy P, Grace Rathnam. Fast dissolving tablets - Background, trends & future perspectives: A review. *International Journal of Review and Life Sciences* 2011, 1(3), 88-96.
93. Saravanakumar K, Jayachandra Reddy P, Chandra Sekhar KB. Recent approaches in mucoadhesive microsphere drug delivery system: A review. *Journal of Innovative Trends in Pharmaceutical Sciences* 2011, 2(3), 77-91.