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MODERN TRENDS IN PHARMACEUTICAL ANALYSIS: INTEGRATION OF HPLC, UPLC, UV, AND SEC-MALLS FOR DRUG PRODUCT EVALUATION

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Abstract

Modern pharmaceutical analysis increasingly relies on advanced multidimensional analytical techniques for comprehensive characterization of drug substances, drug products, biopharmaceuticals, and nanomedicine formulations. High-Performance Liquid Chromatography (HPLC), Ultra-Performance Liquid Chromatography (UPLC), UV-visible spectroscopy, and Size Exclusion Chromatography coupled with Multi-Angle Laser Light Scattering (SEC-MALLS) have emerged as highly powerful analytical platforms because of their sensitivity, selectivity, reproducibility, and broad pharmaceutical applicability. HPLC and UPLC are extensively utilized for assay determination, impurity profiling, dissolution testing, degradation studies, stability-indicating analysis, and pharmaceutical quality control, while UV-visible spectroscopy provides rapid and economical quantitative estimation of pharmaceutical compounds containing chromophoric functional groups. SEC-MALLS additionally enables absolute molecular weight determination, aggregation profiling, conformational analysis, and structural characterization of proteins, monoclonal antibodies, biosimilars, nanoparticles, liposomes, and advanced drug delivery systems without dependence on calibration standards. Integration of orthogonal analytical techniques significantly improves analytical reliability, multidimensional characterization capability, impurity identification, and structural elucidation in complex pharmaceutical formulations. The present review comprehensively discusses the principles, instrumentation, pharmaceutical applications, analytical advantages, method development strategies, validation requirements, regulatory significance, and future perspectives of HPLC, UPLC, UV-visible spectroscopy, and SEC-MALLS in modern pharmaceutical analysis. Particular emphasis is placed on multidetector analytical systems, integrated analytical workflows, pharmaceutical quality assessment, biosimilar evaluation, nanotechnology applications, and regulatory quality control. Emerging advancements involving AI-assisted analytics, automated multidetector platforms, high-resolution chromatography, and real-time process monitoring are also highlighted.

Keywords: *HPLC, UPLC, UV-visible spectroscopy, SEC-MALLS, Pharmaceutical analysis, Drug product evaluation, Hyphenated analytical techniques.*

INTRODUCTION

Pharmaceutical analytical science has undergone remarkable evolution over the past several decades, with the development of highly sensitive, selective, and multidimensional analytical techniques for drug substance and drug product evaluation. Traditional analytical methods initially relied on simple titrimetric, gravimetric, and spectrophotometric approaches; however, the increasing complexity of pharmaceutical formulations, biopharmaceuticals, nanomedicines, and regulatory expectations has driven the advancement of sophisticated chromatographic and spectroscopic analytical technologies [1]. High-Performance Liquid Chromatography (HPLC), Ultra-Performance Liquid Chromatography (UPLC), UV-visible spectroscopy, and Size Exclusion Chromatography coupled with Multi-Angle Laser Light Scattering (SEC-MALLS) have emerged as some of the most widely utilised analytical platforms in modern pharmaceutical industries because of their high sensitivity, reproducibility, accuracy, and broad applicability in pharmaceutical characterisation [2]. These techniques play critical roles in assay determination,

impurity profiling, degradation studies, dissolution testing, molecular weight determination, aggregation analysis, structural characterization, and stability assessment of pharmaceutical and biopharmaceutical products.

The increasing complexity of therapeutic products, including monoclonal antibodies, peptides, proteins, biosimilars, lipid nanoparticles, polymeric drug delivery systems, and nanomedicines, has created significant demand for advanced drug product characterisation techniques capable of providing comprehensive physicochemical and structural information [3]. Conventional single-detector analytical methods frequently fail to adequately characterise molecular heterogeneity, aggregation behaviour, degradation pathways, and conformational stability of complex pharmaceutical systems. Consequently, modern pharmaceutical analysis increasingly relies on integrated analytical platforms combining chromatographic separation with multidetector and spectroscopic detection systems for simultaneous qualitative and quantitative characterisation. HPLC and UPLC are extensively employed for high-resolution separation, impurity profiling, assay analysis, and stability-indicating studies, while UV spectroscopy provides rapid and cost-effective quantitative analysis of pharmaceutical compounds containing chromophoric functional groups [4]. SEC-MALLS has additionally emerged as a highly advanced analytical platform for absolute molecular weight determination, aggregation analysis, and structural characterisation of proteins, polymers, and nanoparticle-based formulations without dependence on calibration standards.Integration of multiple analytical techniques has become increasingly important in pharmaceutical industries because no single analytical method can provide complete physicochemical and structural information regarding complex drug products [5]. Orthogonal analytical approaches involving HPLC, UPLC, UV spectroscopy, and SEC-MALLS enable comprehensive characterisation of purity, potency, molecular weight distribution, particle size, aggregation state, conformational stability, and degradation behaviour in pharmaceutical formulations. These integrated analytical platforms support quality-by-design approaches, regulatory compliance, process optimization, stability assessment, and lifecycle management of pharmaceutical products. Furthermore, regulatory agencies including the United States Food and Drug Administration and International Council for Harmonisation of Technical Requirements for Pharmaceuticals for Human Use increasingly emphasize the use of scientifically validated multidimensional analytical methods to ensure product quality, consistency, and patient safety [6]. Therefore, the present review comprehensively discusses the principles, instrumentation, applications, method development strategies, analytical advantages, regulatory significance, and future perspectives of HPLC, UPLC, UV spectroscopy, and SEC-MALLS in modern pharmaceutical analysis with particular emphasis on integrated analytical approaches for drug product evaluation.

FUNDAMENTALS OF MODERN PHARMACEUTICAL ANALYTICAL TECHNIQUES

Modern pharmaceutical analysis relies heavily on advanced analytical platforms capable of providing accurate qualitative and quantitative information regarding drug substances, impurities, degradation products, biomolecules, and complex pharmaceutical formulations. Among these analytical technologies, High-Performance Liquid Chromatography (HPLC), Ultra-Performance Liquid Chromatography (UPLC), UV-visible spectroscopy, and Size Exclusion Chromatography coupled with Multi-Angle Laser Light Scattering (SEC-MALLS) are extensively utilized because of their high analytical sensitivity, selectivity, reproducibility, and broad applicability in pharmaceutical characterization [7]. High-Performance Liquid Chromatography (HPLC) is a chromatographic technique based on differential partitioning of analytes between stationary and mobile phases under high pressure conditions. Separation occurs because analytes interact differently with the stationary phase according to polarity, hydrophobicity, ionic interactions, and molecular structure, resulting in distinct retention times [8]. HPLC is widely employed for assay analysis, impurity profiling, dissolution testing, stability studies, and quantitative pharmaceutical analysis because of its excellent separation efficiency and analytical precision. Ultra-Performance Liquid Chromatography (UPLC) represents an advanced form of liquid chromatography utilizing sub-2 µm particle size columns and higher operating pressures to achieve significantly improved chromatographic resolution, shorter analysis time, enhanced sensitivity, and reduced solvent consumption compared with conventional HPLC systems [9]. UPLC has become highly valuable for high-throughput pharmaceutical analysis, bioanalysis, forced degradation studies, and complex impurity profiling because of its superior chromatographic performance and rapid analytical capability.

UV-visible spectroscopy remains one of the most widely applied analytical techniques in pharmaceutical industries because of its simplicity, rapid analysis, cost-effectiveness, and applicability for quantitative estimation of compounds containing chromophoric functional groups [10]. The principle of UV spectroscopy is based on the absorption of ultraviolet or visible radiation by molecules, resulting in electronic transitions between molecular orbitals. The absorbance of radiation follows Beer–Lambert's law and is directly proportional to analyte concentration and optical path length. UV spectroscopy is commonly employed for assay determination, dissolution monitoring, kinetic studies, stability evaluation, and simultaneous estimation of pharmaceutical compounds. Despite its simplicity, UV spectroscopy often lacks structural specificity for complex formulations and, therefore is frequently integrated with chromatographic separation techniques such as HPLC and UPLC for enhanced selectivity and analytical reliability [11]. SEC-MALLS represents a highly advanced multidetector analytical platform combining Size Exclusion Chromatography (SEC) with Multi-Angle Laser Light Scattering (MALLS) for simultaneous molecular separation and absolute molecular weight determination [12]. SEC separates analytes according to hydrodynamic volume using porous stationary phases, whereas MALLS measures scattered laser light intensity at multiple angles to determine molecular weight, radius of gyration,

aggregation profile, and molecular conformation without dependence on calibration standards. SEC-MALLS is particularly important for characterization of proteins, monoclonal antibodies, polymers, biosimilars, nanoparticles, liposomes, and advanced nanomedicine formulations because it provides detailed structural and aggregation information under native solution conditions.

Comparative analytical performance among HPLC, UPLC, UV spectroscopy, and SEC-MALLS depends on analytical objectives, sample complexity, sensitivity requirements, and structural characterization needs. HPLC provides robust and versatile separation capability for routine pharmaceutical analysis, whereas UPLC offers superior chromatographic resolution, faster analysis, and enhanced sensitivity. UV spectroscopy provides rapid and economical quantitative analysis but possesses limited structural specificity. SEC-MALLS uniquely enables absolute molecular weight determination, aggregation analysis, and multidimensional structural characterisation of biomolecules and nanomedicine systems [13]. Integration of these analytical techniques, therefore, enables comprehensive pharmaceutical characterisation involving impurity profiling, quantitative estimation, molecular weight determination, conformational analysis, and structural evaluation for modern pharmaceutical and biopharmaceutical products.

Table 01: Comparison of HPLC, UPLC, UV, and SEC-MALLS

Technique	Principle	Major Application	Advantages	Limitations
HPLC	Separation based on analyte interaction with stationary phase	Assay and impurity analysis	High reproducibility	Longer run time
UPLC	High-pressure chromatography using sub-2 µm particles	High-throughput analysis	Faster separation and higher sensitivity	Expensive instrumentation
UV Spectroscopy	Absorption of UV-visible radiation	Quantitative drug analysis	Simple and economical	Limited specificity
SEC-MALLS	Size-based separation with light scattering detection	Molecular weight and aggregation analysis	Absolute molecular weight determination	High instrumentation cost

HIGH-PERFORMANCE LIQUID CHROMATOGRAPHY (HPLC)

High-Performance Liquid Chromatography (HPLC) is one of the most widely utilized analytical techniques in pharmaceutical industries because of its high separation efficiency, reproducibility, sensitivity, and versatility for qualitative and quantitative analysis of pharmaceutical compounds. The HPLC system primarily consists of solvent reservoirs, high-pressure pumps, sample injectors, chromatographic columns, detectors, and computerized data acquisition systems. Separation of analytes occurs through differential interactions between analytes, mobile phase, and stationary phase packed inside chromatographic columns [14]. Various stationary phases, including C18, C8, cyano, phenyl, amino, and ion-exchange phases, are extensively employed depending on analyte polarity, hydrophobicity, and chemical properties. Mobile phase optimisation plays a critical role in chromatographic performance because solvent composition, pH, buffer concentration, gradient profile, and flow rate significantly influence retention behaviour, resolution, peak symmetry, and analytical sensitivity [15]. HPLC has extensive pharmaceutical applications, including assay determination, impurity profiling, stability-indicating analysis, dissolution studies, degradation product identification, pharmacokinetic evaluation, and related substances analysis. Stability-indicating HPLC methods are particularly important because they enable separation and quantification of active pharmaceutical ingredients from degradation products generated under stress conditions such as heat, oxidation, hydrolysis, and photolysis [16]. HPLC is also extensively utilized for dissolution testing, forced degradation studies, and quality control evaluation because of its excellent analytical precision and regulatory acceptance in the pharmaceutical industries.

Applications of HPLC

- Assay analysis
- Dissolution studies
- Degradation studies
- Related substances analysis
- Stability-indicating methods
- Impurity profiling
- Content uniformity testing
- Pharmacokinetic analysis
- Cleaning validation
- Pharmaceutical quality control

ULTRA-PERFORMANCE LIQUID CHROMATOGRAPHY (UPLC)

Ultra-Performance Liquid Chromatography (UPLC) represents an advanced chromatographic technology developed to achieve superior chromatographic resolution, increased sensitivity, shorter analysis time, and reduced solvent consumption compared with conventional HPLC systems. UPLC utilises sub-2 µm particle size stationary phases and operates at significantly higher pressures, thereby improving separation efficiency and peak capacity [17]. Advanced column technology used in UPLC systems provides enhanced mass transfer kinetics and sharper chromatographic peaks, resulting in improved analytical sensitivity and reduced run times. Reduced particle size additionally enables high-resolution separation of structurally similar impurities, degradation products, metabolites, and complex pharmaceutical mixtures [18]. UPLC has become increasingly important in pharmaceutical analysis because of its ability to perform rapid and highly sensitive analytical separations suitable for high-throughput laboratories and regulatory quality control applications. The technique is extensively applied in bioanalysis, forced degradation studies, pharmaceutical quality control, dissolution testing, impurity profiling, and pharmacokinetic investigations. Sensitivity improvements obtained with UPLC enable the detection of low-level impurities and trace degradation products that may not be adequately resolved using conventional HPLC systems. Additionally, UPLC significantly reduces solvent consumption and analysis time, thereby improving laboratory productivity and reducing operational costs [19].

Applications of UPLC

- Bioanalysis
- Forced degradation studies
- Pharmaceutical quality control
- High-throughput analysis
- Trace impurity analysis
- Pharmacokinetic studies
- Stability testing
- Metabolite profiling
- Dissolution testing
- Cleaning validation

Table 02: Comparison of HPLC and UPLC

Parameter	HPLC	UPLC
Particle size	3–5 µm	<2 µm
Operating pressure	Moderate	Very high
Analysis time	Longer	Shorter
Resolution	Moderate	High
Sensitivity	Moderate	High
Solvent consumption	Higher	Lower
Throughput	Moderate	High
Peak capacity	Lower	Higher

UV-VISIBLE SPECTROSCOPY IN PHARMACEUTICAL ANALYSIS

UV-visible spectroscopy is one of the simplest, most economical, and widely utilized analytical techniques in pharmaceutical industries for qualitative and quantitative estimation of pharmaceutical compounds containing chromophoric functional groups [20]. The analytical principle of UV-visible spectroscopy is based on absorption of ultraviolet or visible radiation by molecules resulting in electronic transitions between molecular orbitals. Chromophores such as aromatic rings, conjugated double bonds, carbonyl groups, and heteroatom-containing functional groups absorb radiation within characteristic wavelength regions and therefore enable quantitative analysis based on Beer–Lambert's law [21]. UV-visible spectroscopy is extensively employed for quantitative pharmaceutical analysis because absorbance is directly proportional to analyte concentration and optical path length. The technique is highly valuable for routine drug assay, dissolution monitoring, stability studies, simultaneous estimation of multicomponent formulations, and kinetic analysis because of its simplicity, rapid analysis, and cost-effectiveness. Method validation parameters, including linearity, accuracy, precision, specificity, robustness, and sensitivity are evaluated according to regulatory expectations to ensure analytical reliability [22]. Simultaneous estimation techniques including derivative spectroscopy, ratio spectra methods, and multicomponent analysis have significantly expanded the applicability of UV spectroscopy for complex pharmaceutical formulations and combination drug products.

APPLICATIONS OF UV-VISIBLE SPECTROSCOPY

- Drug assay
- Dissolution monitoring
- Stability studies

- Kinetic studies
- Simultaneous estimation
- Quantitative pharmaceutical analysis
- Drug content determination
- Method validation
- Cleaning verification
- Routine quality control

SEC-MALLS IN DRUG PRODUCT CHARACTERIZATION

Size Exclusion Chromatography coupled with Multi-Angle Laser Light Scattering (SEC-MALLS) is an advanced multidetector analytical platform widely utilized for molecular weight determination, aggregation profiling, and structural characterization of complex pharmaceutical and biopharmaceutical products [23]. SEC-MALLS combines chromatographic separation based on hydrodynamic volume with light scattering detection for direct determination of absolute molecular weight without dependence on calibration standards. The technique provides detailed information regarding molecular weight distribution, aggregation behavior, radius of gyration, molecular conformation, and structural heterogeneity in proteins, polymers, nanoparticles, and advanced drug delivery systems [24]. SEC-MALLS has become particularly important for biopharmaceutical analysis because aggregation and oligomerization significantly influence product stability, therapeutic efficacy, and immunogenicity of monoclonal antibodies, peptides, proteins, and biosimilars. The technique additionally enables structural characterization and aggregation profiling of nanoparticles, liposomes, dendrimers, lipid nanoparticles, and polymeric drug delivery systems under native solution conditions [25]. SEC-MALLS therefore serves as a powerful analytical platform for comprehensive drug product characterization, stability assessment, quality control, and regulatory evaluation in pharmaceutical industries.

APPLICATIONS OF SEC-MALLS

- Monoclonal antibody characterization
- Protein aggregation analysis
- Nanomedicine characterization
- Liposome analysis
- Biosimilar comparability studies
- Molecular weight determination
- Oligomer profiling
- Structural characterization
- Nanoparticle aggregation analysis
- Stability assessment

INTEGRATION OF ANALYTICAL TECHNIQUES FOR DRUG PRODUCT EVALUATION

Integration of analytical techniques has become an essential strategy in modern pharmaceutical analysis because no single analytical platform can provide complete physicochemical, structural, qualitative, and quantitative information for complex pharmaceutical and biopharmaceutical products. Orthogonal analytical approaches involving chromatographic, spectroscopic, and multidetector systems significantly improve analytical reliability, specificity, sensitivity, and structural characterization capability during pharmaceutical evaluation. Multi-technique characterization enables simultaneous assessment of purity, potency, molecular weight distribution, aggregation behavior, degradation pathways, particle size, and conformational stability in pharmaceutical formulations. Complementary analytical information obtained from integrated systems improves impurity identification, structural elucidation, and quality assessment of drug substances and drug products. HPLC combined with UV detection remains one of the most widely employed analytical systems for assay determination, impurity profiling, dissolution studies, and stability-indicating analysis because UV detection provides rapid quantitative estimation following chromatographic separation . UPLC-MS integration provides highly sensitive and high-resolution analysis for trace impurities, metabolites, degradation products, and pharmacokinetic investigations through combined chromatographic separation and mass spectrometric identification. SEC-MALLS multidetector systems integrate light scattering, refractive index, UV, and dynamic light scattering detectors for simultaneous molecular weight determination, aggregation profiling, structural characterization, and nanoparticle analysis [26,27]. Combined impurity and structural analysis using multidimensional analytical platforms therefore supports comprehensive pharmaceutical characterization, quality-by-design approaches, regulatory compliance, and advanced product development strategies in pharmaceutical industries.

APPLICATIONS IN PHARMACEUTICAL INDUSTRIES

Integrated analytical techniques such as HPLC, UPLC, UV-visible spectroscopy, SEC-MALLS, and multidetector hyphenated systems play a central role in pharmaceutical industries for comprehensive characterization, quality control, stability evaluation, and regulatory assessment of pharmaceutical products. Small molecule pharmaceutical analysis

extensively utilizes HPLC and UPLC for assay determination, impurity profiling, dissolution studies, and degradation product analysis because of their high separation efficiency and analytical precision. Biopharmaceutical characterization increasingly depends on SEC-MALLS and multidetector analytical systems for evaluation of molecular weight distribution, aggregation behavior, conformational stability, and biosimilar comparability. Biosimilar evaluation requires highly sensitive orthogonal analytical techniques capable of demonstrating structural equivalence and batch consistency relative to reference products. Nanotechnology-based formulations including polymeric nanoparticles, lipid nanoparticles, liposomes, and nanomedicine systems additionally require multidimensional characterisation involving particle size determination, aggregation analysis, and structural evaluation. Stability studies performed under stress conditions such as temperature, oxidation, humidity, and photolysis are also extensively supported by integrated analytical systems for monitoring degradation pathways and product stability [6]. Regulatory quality control laboratories utilize validated multidetector analytical platforms to ensure compliance with pharmacopeial specifications, GMP requirements, and international regulatory expectations for pharmaceutical products [28-30].

Table 03: Pharmaceutical Applications of Integrated Analytical Systems

Analytical Technique	Major Pharmaceutical Application
HPLC	Assay and impurity analysis
UPLC	High-throughput pharmaceutical analysis
UV Spectroscopy	Quantitative drug estimation
SEC-MALLS	Molecular weight characterization
UPLC-MS	Trace impurity and metabolite analysis
SEC-DLS	Nanoparticle size analysis
HPLC-UV	Stability-indicating analysis
SEC-RI	Polymer and biomolecule analysis

METHOD DEVELOPMENT AND VALIDATION

Method development and validation are critical components of pharmaceutical analysis because analytical methods must provide accurate, precise, reproducible, and regulatory-compliant results for routine quality assessment and pharmaceutical characterisation. Analytical method optimisation involves careful selection of chromatographic conditions, including stationary phase chemistry, mobile phase composition, buffer concentration, pH, flow rate, column temperature, and detector parameters, to achieve adequate resolution, peak symmetry, sensitivity, and analytical reliability. Accuracy and precision studies are performed to ensure the correctness and repeatability of analytical measurements under multiple experimental conditions. Specificity evaluation confirms the ability of analytical methods to distinguish analytes from impurities, degradation products, excipients, and matrix interferences. Sensitivity assessment determines the lowest detectable and quantifiable analyte concentrations, whereas robustness studies evaluate method stability following small deliberate variations in chromatographic or instrumental parameters. Regulatory agencies including the International Council for Harmonisation of Technical Requirements for Pharmaceuticals for Human Use, require analytical method validation according to internationally accepted guidelines to ensure data integrity, reproducibility, and pharmaceutical quality control compliance. Consequently, validated analytical methods are essential for pharmaceutical development, stability studies, batch release testing, and regulatory submissions [31-33].

ADVANTAGES AND LIMITATIONS

Modern pharmaceutical analytical techniques including HPLC, UPLC, UV-visible spectroscopy, SEC-MALLS, and multidetector hyphenated systems offer several important analytical advantages for pharmaceutical characterization and quality assessment. These techniques provide high analytical sensitivity, enabling detection of trace impurities, degradation products, aggregates, and structurally heterogeneous species in complex pharmaceutical formulations. Multi-parameter analysis obtained through integrated detector systems allows simultaneous evaluation of molecular weight, particle size, aggregation behavior, structural conformation, assay content, and impurity profile in a single analytical run. Improved chromatographic resolution achieved using advanced stationary phases and high-pressure systems significantly enhances separation efficiency for closely related compounds and degradation products. Faster analysis time, particularly with UPLC systems, improves laboratory productivity and reduces solvent consumption and operational costs . Despite these advantages, several analytical limitations remain important considerations. High instrumentation cost and maintenance requirements limit accessibility of advanced multidetector systems in smaller laboratories. Complex method optimization involving multiple chromatographic and detector parameters often requires extensive analytical expertise and experimental development. Data interpretation challenges associated with multidimensional analytical datasets additionally necessitate advanced computational software and skilled analytical

scientists. Nevertheless, continuous technological advancements continue to improve analytical performance, automation, and accessibility of integrated pharmaceutical analytical systems [34,35].

Table 05: Advantages and Limitations of Pharmaceutical Analytical Techniques

Technique	Advantages	Limitations
HPLC	Robust and reliable	Longer analysis time
UPLC	Faster and highly sensitive	High operating pressure
UV Spectroscopy	Simple and economical	Limited specificity
SEC-MALLS	Absolute molecular characterization	Expensive instrumentation
UPLC-MS	Trace-level impurity detection	Complex data interpretation

CONCLUSION

Integration of modern analytical techniques including HPLC, UPLC, UV-visible spectroscopy, SEC-MALLS, and multidetector hyphenated systems has significantly transformed pharmaceutical analysis and drug product evaluation. These analytical platforms collectively provide comprehensive qualitative, quantitative, structural, and physicochemical information required for pharmaceutical development, quality control, stability assessment, and regulatory compliance. HPLC and UPLC offer highly efficient chromatographic separation and impurity profiling, while UV spectroscopy provides rapid and economical quantitative analysis. SEC-MALLS additionally enables advanced molecular weight determination, aggregation profiling, and structural characterization of complex biomolecules and nanomedicine systems. Integrated analytical approaches therefore improve analytical reliability, multidimensional characterization capability, and quality-by-design implementation in pharmaceutical industries. Increasing regulatory emphasis on detailed pharmaceutical characterization, biosimilar evaluation, and nanomedicine assessment is expected to further expand the importance of multidetector analytical technologies in modern pharmaceutical sciences. Continuous advancements involving AI-assisted analytics, automated multidetector systems, high-resolution chromatography, and real-time process monitoring will likely enhance analytical sensitivity, data interpretation, and pharmaceutical quality assessment in future pharmaceutical research and industrial applications.

AUTHOR CONTRIBUTIONS

Venkatanarayana Bypaneni conceived and drafted the manuscript. Jayaram Kamma contributed to literature collection, analytical and regulatory sections. Murugesan Palanivelu contributed to manuscript review, editing, and technical revision. All authors approved the final manuscript.

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CONFLICT OF INTEREST

The authors declare no conflict of interest.

ETHICAL APPROVAL

Not applicable.

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