

Pharmaceutical Analysis: Ai, Chemometrics, Spectroscopy and Chromatography for Smart Quality Control

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Graphical Abstract

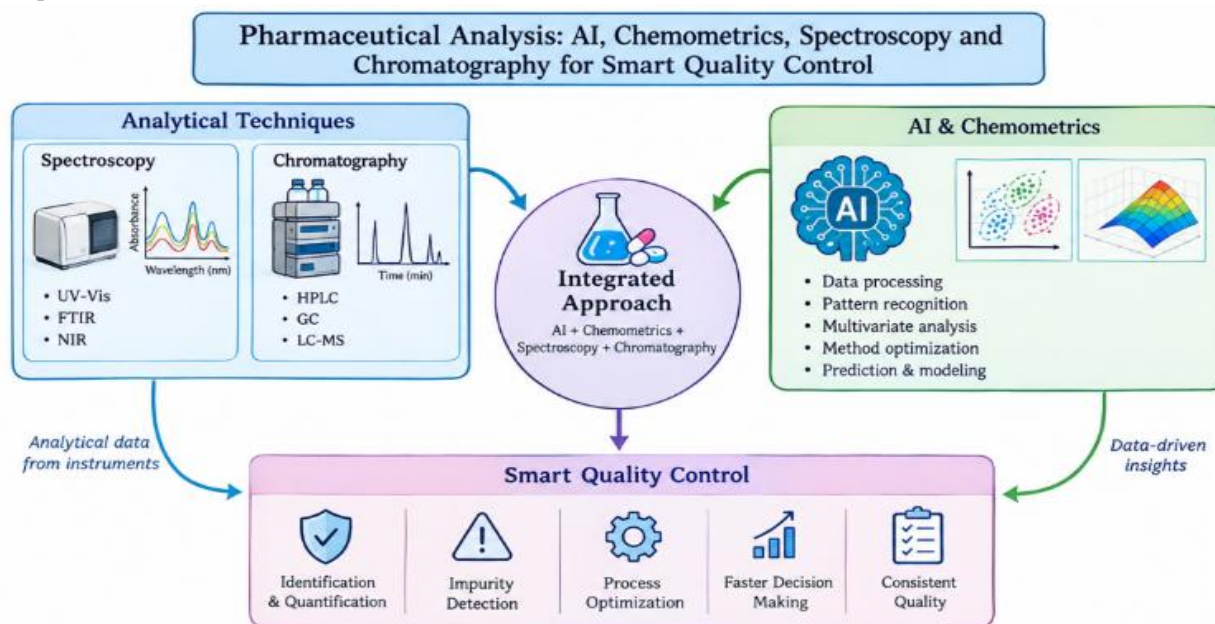


Figure 1. Integrated AI–Chemometrics–Spectroscopy–Chromatography Framework for Smart Pharmaceutical Quality Control. [1,3].

Abstract—Pharmaceutical analysis is undergoing a major transformation through the integration of artificial intelligence (AI), chemometrics, spectroscopy, and chromatography. Conventional analytical techniques generate large and complex datasets that require accurate interpretation, rapid processing, and reliable decision-making. Spectroscopic methods such as

UV–Visible, FTIR, and NIR provide rapid information about chemical composition, while chromatographic techniques including HPLC, GC, and LC–MS enable separation, identification, and quantification of drug substances and impurities. Chemometric tools enhance these analytical approaches by extracting meaningful patterns from multidimensional data and supporting

calibration, classification, and method optimization. AI further extends these capabilities through automated data interpretation, pattern recognition, prediction, anomaly detection, and intelligent quality assessment. Their combined application can improve analytical efficiency, reproducibility, sensitivity, and process monitoring. This review discusses recent developments, applications, advantages, limitations, and future opportunities of integrating these technologies to establish smarter, faster, and data-driven pharmaceutical quality-control systems while supporting safer medicines and more consistent manufacturing outcomes.

***Index Terms*—Pharmaceutical analysis; Artificial intelligence; Chemometrics; Spectroscopy; Chromatography; Smart quality control; Quality assurance.**

I. INTRODUCTION

Pharmaceutical analysis is an essential part of drug development and manufacturing because the identity, strength, purity, safety, and consistency of a pharmaceutical product must be established before it reaches the patient. Conventional quality-control laboratories commonly rely on established analytical procedures such as spectrophotometry, spectroscopy, chromatography, and other instrumental methods. Among these, high-performance liquid chromatography (HPLC) remains an important technique for pharmaceutical quality control because of its ability to provide selective separation and quantitative information for active pharmaceutical ingredients, impurities, and degradation products [1]. However, increasing numbers of samples, complex formulations, stringent quality requirements, and the need for faster analytical decisions have created a demand for more efficient approaches to handling analytical data.

Spectroscopic techniques have attracted considerable attention because they can provide chemical information rapidly and, in many cases, with little or no sample destruction. UV–Visible, Fourier-transform infrared (FTIR), Raman, and near-infrared (NIR) spectroscopy can be applied for identification, quantitative analysis, raw-material assessment, formulation characterization, and process monitoring. NIR spectroscopy, for example, has been investigated for pharmaceutical development, production

monitoring, and quality-control applications because of its rapid and non-destructive nature [2,3]. Recent work also highlights the growing use of NIR methods for real-time monitoring of manufacturing operations such as granulation, drying, tableting, and coating. Although spectroscopic measurements can generate large amounts of useful information, interpretation of complex spectra is not always straightforward. Overlapping signals, baseline variations, instrumental differences, and matrix effects may make direct interpretation difficult. Chemometrics provides a systematic way to convert such multidimensional analytical measurements into useful chemical and quality-related information. Techniques such as principal component analysis (PCA), partial least-squares (PLS) regression, partial least-squares discriminant analysis (PLS-DA), and classification methods can be used for data exploration, calibration, classification, prediction, and detection of unusual samples [4,5]. The combination of spectroscopy and chemometrics has therefore become an important approach for pharmaceutical quality assessment, particularly where rapid and non-destructive measurements are desirable.

Chromatographic analysis provides a complementary analytical perspective. While spectroscopy can rapidly provide chemical fingerprints, chromatographic techniques separate components within a sample and allow individual substances to be identified and quantified. HPLC, gas chromatography (GC), and liquid chromatography coupled with mass spectrometry (LC–MS) are widely relevant to pharmaceutical analysis. Chromatography is particularly valuable for evaluating assay, purity, impurities, degradation products, and complex mixtures. Emerging chromatographic approaches are also being investigated to reduce analysis time, solvent consumption, and environmental burden while maintaining adequate analytical performance [6].

The increasing digitalization of analytical laboratories has created an opportunity to combine these established techniques with artificial intelligence (AI) and machine learning (ML). AI-based approaches can assist with pattern recognition, classification, prediction, spectral interpretation, chromatographic data processing, and optimization of analytical conditions. Recent literature describes applications of AI to spectroscopic and chromatographic datasets, including automated interpretation and prediction of

analytical responses [7]. AI can therefore act as an additional layer between analytical measurement and quality-related decision-making rather than replacing the underlying analytical technique.

The integration of AI, chemometrics, spectroscopy, and chromatography provides a broader framework for what may be described as smart pharmaceutical quality control. In such a framework, analytical instruments generate experimental data, chemometric approaches organize and interpret complex datasets, and AI-based models can assist with prediction, classification, anomaly detection, and optimization. This integration may support faster identification of atypical samples, improved process understanding, and more efficient use of analytical information. Nevertheless, the reliability of these systems depends strongly on the quality and representativeness of the underlying data, appropriate model development, validation, interpretability, and control of model performance. Recent discussions of AI in analytical chemistry emphasize data quality, model interpretation, and integration as important challenges for practical implementation.[8]

From a regulatory perspective, advanced analytical approaches still need to demonstrate that they are fit for their intended purpose. ICH Q2(R2) establishes principles for validation of analytical procedures, including assessment of characteristics such as specificity, accuracy, precision, and other performance parameters. ICH Q14 further provides a framework for science- and risk-based analytical procedure development [9]. These principles are particularly relevant when multivariate, spectroscopic, or AI-assisted analytical models are incorporated into pharmaceutical quality systems. The U.S. FDA has also discussed risk-based approaches for establishing the credibility of AI models used to support regulatory decision-making for drug quality and other areas [10]. Therefore, the convergence of advanced instrumentation, multivariate analysis, and AI represents an important development in pharmaceutical analysis. Rather than considering spectroscopy, chromatography, chemometrics, and AI as separate technologies, their complementary roles can be examined as components of a connected analytical workflow. This review focuses on the principles, applications, advantages, limitations, validation requirements, and future prospects of this

integrated approach, with particular emphasis on its potential to support accurate, efficient, data-driven, and reliable pharmaceutical quality control.[11]

II. EVOLUTION OF PHARMACEUTICAL QUALITY CONTROL

Pharmaceutical quality control has traditionally relied on validated analytical procedures to establish the identity, strength, purity, stability, and consistency of pharmaceutical materials. HPLC, GC, UV-Visible spectroscopy, and infrared spectroscopy remain important because they provide established approaches for identification and quantitative analysis. The development of Quality by Design (QbD), Process Analytical Technology (PAT), and continuous manufacturing has broadened the role of analytical testing from final-product confirmation toward process understanding and real-time monitoring [12].

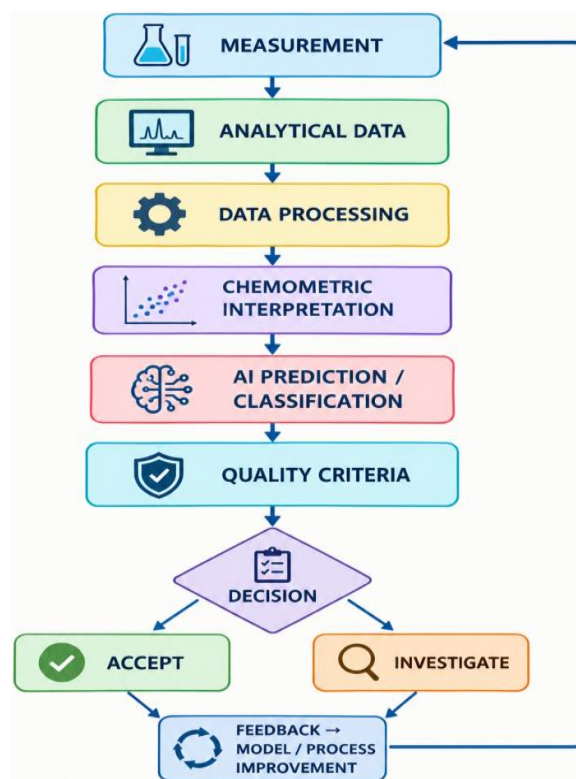


Figure 2. Original conceptual decision cycle illustrating how analytical measurements can be processed through chemometric and AI models to support pharmaceutical quality assessment and continuous improvement. [6–10]

NIR and Raman spectroscopy are particularly relevant to this transition because rapid measurements can be

obtained during processing when suitable instrumentation and calibration models are available [13]. Chemometric modelling then converts complex instrumental responses into useful information about quality attributes. AI and ML can further support prediction and classification when adequate datasets and validated workflows are available [14]. Thus, smart quality control can be viewed as a sequence of measurement, data processing, modelling, prediction, and quality decision.

III. SPECTROSCOPY IN PHARMACEUTICAL ANALYSIS

Spectroscopy provides chemical and physical information through the interaction of electromagnetic radiation with matter. Important techniques in pharmaceutical analysis include UV–Visible, FTIR, NIR, Raman, fluorescence, and NMR spectroscopy. Each technique provides different types of molecular information and can therefore be selected according to the analytical objective [15].

Spectroscopic methods are attractive for rapid pharmaceutical analysis because some measurements can be performed with limited sample preparation. NIR and Raman have also been investigated extensively for process monitoring and PAT applications [16].

3.1 UV–Visible Spectroscopy

UV–Visible spectroscopy is widely used for quantitative pharmaceutical analysis because of its accessibility and suitability for compounds that absorb in the ultraviolet or visible region. Applications include assay determination, dissolution testing, degradation studies, and simultaneous estimation. A limitation arises when several components have overlapping absorption bands. Multivariate methods can address this problem by using information across multiple wavelengths rather than relying on one analytical signal [17].

3.2 FTIR Spectroscopy

Fourier-transform infrared (FTIR) spectroscopy provides molecular information related to vibrational transitions and can generate characteristic spectral fingerprints. Pharmaceutical applications include API identification, excipient characterization, raw-material verification, compatibility studies, and investigation of

structural changes. Chemometric methods such as PCA, PLS, PLS-DA, and SIMCA can assist with interpretation when spectral bands overlap [18].

3.3 Near-Infrared Spectroscopy

Near-infrared spectroscopy is an important tool for modern pharmaceutical quality control. It has been investigated for raw-material identification, quantitative analysis, moisture measurement, blend uniformity, granulation, drying, tablet analysis, coating, and process monitoring [19]. NIR spectra commonly contain broad and overlapping bands, so mathematical preprocessing and multivariate calibration are often required to convert spectral information into reliable predictions [20].

3.4 Raman Spectroscopy

Raman spectroscopy provides molecular information through inelastic light scattering and has been investigated for pharmaceutical identification, formulation analysis, polymorph characterization, process monitoring, and PAT [3]. Combining Raman information with chemometric or machine-learning methods can assist with interpretation of complex spectra, classification, and monitoring of process changes.

IV. CHEMOMETRICS IN PHARMACEUTICAL ANALYSIS

Chemometrics applies mathematical, statistical, and computational methods to chemical measurements. Its importance has increased with the availability of multidimensional data from modern analytical instruments. Chemometric approaches support data preprocessing, exploratory analysis, classification, quantitative prediction, calibration, pattern recognition, experimental design, and model validation [20].

4.1 Principal Component Analysis

Principal Component Analysis (PCA) is an unsupervised multivariate method that reduces the dimensionality of complex datasets while retaining major patterns of variation. In pharmaceutical analysis, PCA can support exploratory data analysis, visualization of sample relationships, investigation of batch variability, and identification of unusual observations [21].

4.2 Partial Least Squares Regression

Partial Least Squares (PLS) regression establishes quantitative relationships between instrumental measurements and reference analytical values. It is commonly used for NIR and other spectroscopic calibration problems involving API concentration, moisture, blend composition, and physical properties. Model performance depends on representative calibration samples, appropriate preprocessing, and independent validation [22].

4.3 Classification Methods

Classification methods assign samples to predefined groups based on their analytical characteristics. Examples include PLS-DA, SIMCA, support vector machines, random forests, and artificial neural networks. Potential applications include raw-material identification, batch discrimination, product classification, and screening of atypical samples [6,23].

V. ARTIFICIAL INTELLIGENCE IN PHARMACEUTICAL ANALYSIS

Artificial intelligence and machine learning are increasingly being explored for pharmaceutical analytical applications because modern instruments generate large and complex datasets. Potential uses include spectral classification, quantitative prediction, chromatographic optimization, peak interpretation, anomaly detection, impurity assessment, and process monitoring [24].

AI-assisted analysis should be treated as a component of an analytical procedure rather than as an independent replacement for scientific validation. Training data should be representative, models should be appropriately validated, and predictions should be

experimentally confirmed when required for regulated quality decisions [25].

VI. CHROMATOGRAPHY IN PHARMACEUTICAL QUALITY CONTROL

Chromatography remains a fundamental technology in pharmaceutical quality control because it separates components in complex samples and allows individual detection and quantification.

Major approaches include HPLC, UHPLC, GC, HPTLC, supercritical fluid chromatography, LC-MS, and GC-MS. HPLC and UHPLC are widely used for assay, impurity analysis, degradation studies, and stability investigations.

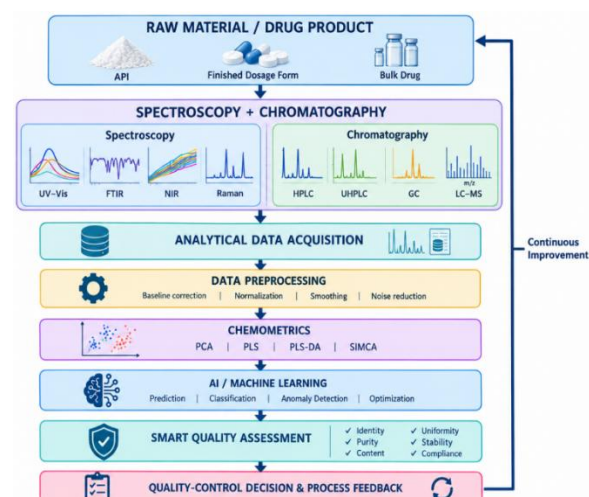


Figure 3. Original conceptual framework showing the integration of spectroscopic and chromatographic measurements with chemometric and AI-based data analysis for pharmaceutical quality control. [1–8]

Chromatographic data can also be combined with chemometric methods to compare complete fingerprints rather than only individual peaks [26].

Table 1. Conventional versus Smart Pharmaceutical Quality Control [26,27]

Parameter	Conventional QC	Smart QC
Primary focus	Finished-product testing	Product and process information
Data	Individual measurements	Multidimensional data
Interpretation	Mainly analyst-driven	Analyst + computational models
Spectroscopy	Identification/quantification	Multivariate monitoring
Chromatography	Separation/quantification	Separation + data modelling
Chemometrics	Selected applications	Integrated modelling
AI	Limited	Prediction/classification
Process monitoring	Periodic	Potentially continuous
Decision support	Manual	Data-assisted

6.1 HPLC

High-performance liquid chromatography is one of the principal techniques used for pharmaceutical quality control. Important method parameters include stationary phase, mobile-phase composition, pH, flow rate, temperature, gradient conditions, and detection wavelength. These variables influence retention, selectivity, resolution, peak shape, and analysis time. Design of experiments and computational modelling can assist method development by examining relationships between method variables and analytical responses [27].

VII. AI-ASSISTED CHROMATOGRAPHIC ANALYSIS

Chromatographic datasets contain multiple variables, including retention time, peak area, peak height, peak width, resolution, and peak shape. These variables can

be used in multivariate modelling. AI and ML approaches may assist with retention prediction, chromatographic condition optimization, peak identification, impurity classification, and anomaly detection [10]. Computational predictions should be experimentally verified before they are incorporated into a regulated analytical procedure.

VIII. CHROMATOGRAPHIC FINGERPRINTING AND CHEMOMETRICS

Chromatographic fingerprinting considers the overall analytical pattern rather than relying on a single peak. Variables such as retention time, peak area, peak intensity, peak width, and peak ratios can be used for multivariate comparison. Potential applications include batch comparison, stability monitoring, impurity-pattern assessment, product classification, and detection of atypical samples [28].

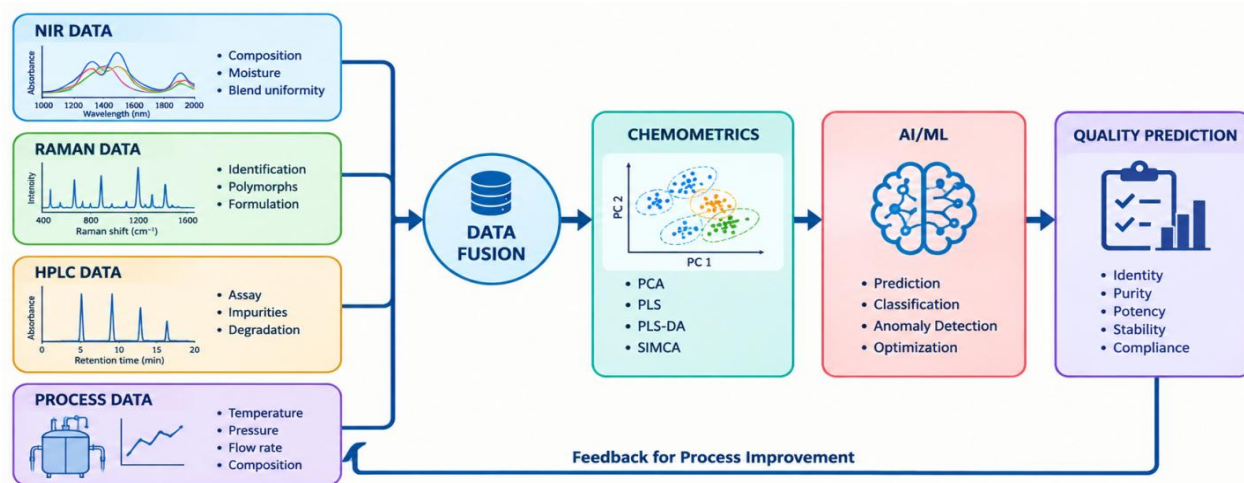


Figure 3. Proposed conceptual strategy for combining spectroscopic, chromatographic, and process information through multivariate and AI-based analysis. [27]

IX. HYPHENATED ANALYTICAL TECHNIQUES

Hyphenated techniques combine chromatographic separation with an additional detection or structural characterization method. Examples include HPLC-DAD, HPLC-FLD, LC-MS, GC-MS, and LC-NMR. Chromatography provides separation while the coupled detector contributes additional chemical or structural information. LC-MS and GC-MS are particularly valuable for trace components, impurities, degradation products, and other compounds requiring structural characterization.[29]

X. PROCESS ANALYTICAL TECHNOLOGY

Process Analytical Technology focuses on obtaining timely information about pharmaceutical processes and using that information to improve process understanding and control. NIR and Raman have been investigated within PAT because they can provide rapid measurements and can potentially be implemented using process probes [11]. Applications include blending, granulation, drying, compression, coating, and continuous manufacturing.

XI. ANALYTICAL QUALITY BY DESIGN

Analytical Quality by Design (AQbD) applies systematic development principles to analytical procedures. A general workflow includes definition of the Analytical Target Profile, risk assessment,

identification of critical method parameters, experimental design, statistical modelling, optimization, validation, and lifecycle monitoring. AQbD can be combined with chemometric and AI approaches to investigate relationships between analytical conditions and method performance [30].

Table 2. Comparison of Major Analytical Technologies [31]

Technique	Major strength	Pharmaceutical application	Major limitation
UV–Visible	Simple quantitative measurement	Assay	Spectral overlap
FTIR	Molecular fingerprint	Identification	Overlapping bands
NIR	Rapid, non-destructive analysis	PAT/QC	Calibration requirement
Raman	Molecular information	Identification/PAT	Fluorescence interference
HPLC	High separation capability	Assay/impurity analysis	Solvent and time requirements
GC	Effective separation of volatile compounds	Residual solvents	Limited analyte suitability
LC–MS	High selectivity	Impurity characterization	Cost and complexity
Chemometrics	Multivariate interpretation	Classification/prediction	Model dependency
AI/ML	Prediction and pattern recognition	Smart QC	Data and validation requirements

XII. INTEGRATION OF AI AND CHEMOMETRICS

The combination of AI and chemometrics can create comprehensive analytical workflows. A spectroscopic workflow may progress from spectral acquisition to preprocessing, PCA or PLS, machine-learning modelling, and quality prediction. A chromatographic workflow may progress from HPLC acquisition to peak/data extraction, multivariate analysis, AI modelling, and impurity or quality assessment. The computational component should remain connected to sound analytical principles, appropriate validation, and scientific interpretation [32].

XIII. DATA PREPROCESSING

Data preprocessing is an important stage in spectroscopic and chromatographic modelling. Spectroscopic data may contain baseline variation, noise, scattering, instrumental differences, and overlapping signals.

Common approaches include normalization, smoothing, baseline correction, first and second derivatives, standard normal variate, and

multiplicative scatter correction. The preprocessing method should be selected according to the analytical problem and evaluated during model development [33].

XIV. MODEL VALIDATION

Analytical models should be appropriately validated before they are used for quality-control decisions. Relevant characteristics include accuracy, precision, specificity, robustness, prediction error, calibration performance, and external validation. ICH Q2(R2) provides guidance for validation of analytical procedures and includes considerations relevant to multivariate analytical procedures [34]. High apparent accuracy on training data alone is not sufficient evidence of model reliability.[35]

XV. EXPLAINABLE AI

Some AI models can produce predictions without an easily understandable explanation of how the prediction was generated. In pharmaceutical analysis, explainability can help investigators understand which spectral regions, chromatographic variables, or

analytical features contributed to a prediction. Feature-importance analysis, sensitivity analysis, and related explainability methods may support scientific interpretation. This becomes particularly relevant when AI-generated information contributes to a regulated pharmaceutical quality decision [36].

XVI. APPLICATIONS IN PHARMACEUTICAL QUALITY CONTROL

Table 4. Applications of Smart Analytical Technologies [38,39]

Quality-control requirement	Technique	Computational approach	Expected analytical role
Identity	NIR/Raman/FTIR	PCA/classification	Rapid identification
Assay	UV/NIR/HPLC	PLS/ML	Quantification
Blend uniformity	NIR/Raman	PLS	Process monitoring
Moisture	NIR	PLS	Rapid prediction
Impurities	HPLC/LC-MS	Multivariate analysis	Detection/characterization
Stability	HPLC/UHPLC	Chemometrics	Degradation monitoring
Counterfeit screening	Raman/NIR	Classification	Screening
Continuous manufacturing	NIR/Raman	PAT/ML	Process monitoring

XVII. Advantages of Smart Quality Control

The integration of spectroscopy, chromatography, chemometrics, artificial intelligence (AI), and machine learning (ML) is changing pharmaceutical quality control from a predominantly end-product testing approach toward a more information-driven and process-oriented system. Instead of relying on a single analytical result, smart quality control can combine chemical measurements, process variables, and historical datasets to obtain a broader understanding of product and process behaviour. The FDA Process Analytical Technology (PAT) framework similarly emphasizes timely measurement of critical material and process attributes to improve process understanding and control. [36]

17.1 Rapid and Non-Destructive Analysis

One important advantage is the potential for rapid analysis with limited or no sample preparation. NIR and Raman spectroscopy can provide rapid, non-destructive measurements and can be implemented at-line, on-line, or in-line in suitable pharmaceutical processes.

These techniques can provide both chemical and physical information from a single measurement, making them useful for monitoring raw materials,

Integration of analytical instruments with computational methods can support raw-material identification, assay, blend uniformity, moisture determination, impurity analysis, stability monitoring, counterfeit screening, process monitoring, and real-time quality assessment. NIR and Raman have established research applications in pharmaceutical process monitoring, while chemometrics supports interpretation of multidimensional analytical data [31].

blends, granulation, drying, and other manufacturing operations.

Compared with conventional laboratory procedures that may require sampling, extraction, dilution, separation, and subsequent analysis, spectroscopic measurements can substantially shorten the time between measurement and interpretation when the analytical procedure has been appropriately developed and validated. This characteristic is particularly relevant when rapid process feedback is required. [37]

17.2 Multivariate Interpretation of Complex Data

Pharmaceutical samples often generate complex analytical signals containing information from several components simultaneously. Chemometric techniques such as principal component analysis (PCA), partial least-squares (PLS), PLS-discriminant analysis (PLS-DA), and SIMCA can extract useful patterns from multidimensional datasets. Chemometrics can therefore support identification, classification, calibration, and quantitative analysis when conventional univariate interpretation is insufficient.[37]

For example, an NIR spectrum may contain overlapping signals from an active pharmaceutical ingredient, excipients, moisture, and physical properties of a powder. Chemometric modelling can

relate these spectral variations to reference measurements and thereby generate quantitative or classification models. This makes the combination of spectroscopy and chemometrics particularly useful for pharmaceutical quality applications.[38]

17.3 Real-Time Process Monitoring

Smart analytical systems can support monitoring during manufacturing rather than depending entirely on testing after production has been completed. NIR and Raman instruments can be coupled with fibre-optic probes for measurements directly within or close to the process. Such measurements can provide information about changes occurring during processing and may support timely process adjustments.

This approach is consistent with the PAT concept, in which analytical measurements are integrated with process understanding and control. The objective is not simply to test the final product but to generate information that can help maintain the process within an appropriate operating region.[39]

17.4 Improved Pattern Recognition

AI and ML can process large analytical datasets and identify relationships that may be difficult to recognize using conventional approaches. Depending on the application and quality of available data, supervised and unsupervised methods can be used for classification, prediction, anomaly detection, and process modelling. Recent pharmaceutical literature describes applications of ML to process modelling, critical-quality-attribute prediction, process optimization, and PAT-based monitoring.

For example, a trained model may distinguish between acceptable and unusual analytical patterns or identify observations that require additional investigation. Such systems can be useful for screening and prioritization, although model outputs still require appropriate validation and scientific interpretation before being used for regulated quality decisions.[40]

17.5 Improved Process Understanding

Combining analytical and process information can provide a more complete picture of pharmaceutical manufacturing. Spectroscopic measurements may provide information about composition or physical properties, while process variables such as temperature, pressure, flow rate, mixing conditions, or

processing time provide contextual information. Integration of these datasets can help identify relationships between process conditions and critical quality attributes.

This is particularly relevant to Quality by Design (QbD), where understanding the relationship between material attributes, process parameters, and product quality is an important part of pharmaceutical development.[41]

17.6 Early Detection of Deviations

Another potential benefit is earlier recognition of abnormal process behaviour. Conventional testing may identify a problem after a sample has been collected and analysed. In contrast, continuous or frequent analytical measurements can reveal changes while processing is still occurring. AI or chemometric models can be used to compare current observations with established patterns and identify potential deviations for investigation.

However, an abnormal model output should not automatically be interpreted as product failure. It may result from an instrument issue, sampling variation, changes in raw-material properties, or a model operating outside its calibration domain. Therefore, investigation procedures and human review remain important.[42]

17.7 Data-Assisted Quality Decisions

Smart quality control can combine multiple sources of evidence before a quality decision is made. For example, spectroscopic information can be considered alongside chromatographic results, process parameters, historical batch information, and predefined quality criteria. This approach can provide a more structured basis for investigation and decision support.

Importantly, computational tools should support rather than bypass established analytical controls. ICH Q2(R2) emphasizes that analytical procedures must be demonstrated to be suitable for their intended purpose, while lifecycle changes may require appropriate revalidation or other scientifically justified evaluation.[43]

17.8 Reduced Dependence on Extensive Sample Preparation

For suitable applications, spectroscopic techniques can reduce the need for extraction, dilution, filtration,

and other preparation steps. NIR, for example, has been described as a fast and non-destructive technique that can be applied to solid, liquid, and other pharmaceutical materials.

Reducing sample preparation can potentially decrease analysis time, analyst workload, and opportunities for preparation-related variability. Nevertheless, conventional reference methods remain important for calibration, validation, confirmation, and situations where higher chemical specificity or separation is required.[44]

17.9 Support for Continuous Manufacturing

Smart analytical technologies are particularly relevant to continuous pharmaceutical manufacturing because continuous processes require timely information about material and product quality. Recent literature describes the integration of NIR and Raman with PAT approaches for continuous pharmaceutical manufacturing, with emphasis on real-time monitoring and control.

ML approaches are also being investigated for predictive modelling and real-time process optimization in pharmaceutical manufacturing. Current research, however, identifies challenges including data availability, model interpretability, extrapolation, uncertainty estimation, and integration with existing manufacturing workflows. [45]

17.10 Potential for More Efficient Laboratory Workflows

Automation of repetitive data-processing activities can help analysts manage large numbers of spectra, chromatograms, and process measurements. Automated preprocessing, classification, peak-related analysis, model-based prediction, and anomaly screening may reduce repetitive manual interpretation. Recent reviews describe AI applications across spectroscopic and chromatographic pharmaceutical analysis, although implementation depends strongly on data quality and model validation.[45]

17.11 Better Integration of Different Analytical Techniques

The greatest benefit may arise when complementary techniques are used together rather than independently. For example, NIR can provide rapid information about composition and physical characteristics, Raman can contribute molecular

fingerprint information, and HPLC can provide separated quantitative information about assay and impurities.

Chemometric and AI methods can then help integrate these different datasets.[41]

Such multimodal analysis can provide complementary evidence and may improve the ability to recognize complex quality patterns. However, combining datasets also increases requirements for data synchronization, preprocessing, model validation, and data integrity.[46]

17.12 Regulatory and Quality-System Compatibility

Smart analytical technologies can be incorporated into pharmaceutical quality systems when their intended use, performance, validation, and lifecycle management are appropriately defined. FDA has specific guidance addressing NIR analytical procedures that use chemometric models, while the PAT framework provides a broader basis for innovative process monitoring and control.[46]

Therefore, the use of AI or advanced chemometrics does not eliminate conventional expectations for analytical suitability. Instead, the computational component becomes part of the analytical procedure and should be appropriately controlled according to its intended application.[47]

XVIII. CHALLENGES

Several challenges need to be addressed before smart analytical systems can be routinely adopted. These include data quality, dataset representativeness, overfitting, instrument-to-instrument variability, model transferability, explainability, cybersecurity and data integrity, and regulatory expectations. Recent literature has also identified validation datasets, interpretability, algorithmic bias, and regulatory uncertainty as important considerations for AI-assisted pharmaceutical analysis [48].

XIX. FUTURE PERSPECTIVES

The future of pharmaceutical analysis is likely to involve increasing integration of AI, chemometrics, spectroscopy, chromatography, PAT, and QbD. Potential developments include AI-assisted analytical method development, automated chromatographic optimization, portable spectroscopy, multimodal data

fusion, real-time release testing, automated anomaly detection, explainable AI, and digital analytical laboratories. These developments will require strong validation and lifecycle management to ensure that computational performance translates into reliable analytical decisions [49].

XX. CONCLUSION

The integration of artificial intelligence, chemometrics, spectroscopy, and chromatography is creating new opportunities for pharmaceutical quality control. Spectroscopic techniques such as NIR, Raman, FTIR, and UV-Visible spectroscopy can provide rapid chemical information, while chromatographic techniques remain essential for separation, assay, impurity analysis, and stability-related investigations [44]. Chemometric techniques provide a mathematical framework for interpreting multidimensional analytical datasets, while AI and machine learning can extend these capabilities toward prediction, classification, anomaly detection, and optimization [50]. However, smart quality control should not be based solely on algorithmic performance. Representative datasets, appropriate preprocessing, independent validation, model interpretability, data integrity, and regulatory oversight remain essential for reliable implementation. The combination of established analytical science with carefully validated computational tools therefore represents a practical direction for the development of more data-rich and responsive pharmaceutical quality systems.[51]

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