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INTEGRATION OF CHROMATOGRAPHIC TECHNIQUES USING AI TOOLS

Sufiya.SK[a], *Sai Teja.B[a], E.V.S. Prakash[b], Venkata Suresh.P[a].

[a]Department of Pharmaceutical Analysis, Chalapathi Institute of Pharmaceutical Sciences, Lam, Guntur, A.P, India-522034.

[b]Clians Labs private limited, Hyderabad, Telangana,India-500037

Abstract:

Artificial intelligence (AI) has gained prominence as an effective analytical support tool in modern chromatography, augmenting traditional experimental and statistical methodologies. In contrast to conventional trial-and-error approaches, AI-driven algorithms can process extensive and complex chromatographic datasets, uncover hidden patterns, and facilitate data-driven decision-making. Within chromatographic analysis, AI plays a growing role in automated data processing, peak detection and deconvolution, retention time prediction, and compound identification—particularly for complex mixtures where manual interpretation is labor-intensive and prone to variability

Machine learning (ML) models such as artificial neural networks (ANNs), support vector machines (SVMs), and random forest algorithms are increasingly utilized to optimize chromatographic parameters, including mobile phase composition, flow rate, gradient profile, and column selection. By learning from historical experimental data, these models can predict optimal conditions with fewer experimental trials, thereby enhancing efficiency and conserving resources. AI-assisted peak integration further improves data consistency by reducing operator-dependent variability and enhancing reproducibility across laboratories.

In pharmaceutical research and quality control, AI-enhanced chromatography accelerates method development, impurity profiling, and stability studies. During drug development, it enables rapid formulation screening and real-time monitoring of degradation products. In quality control operations, AI-enabled automation increases throughput while ensuring data integrity. Similarly, environmental and food analyses benefit from AI-assisted chromatographic techniques for trace-level detection and classification of contaminants.

Despite its advantages, regulatory compliance remains a crucial consideration. Algorithm transparency, data traceability, model validation, and adherence to established analytical guidelines are essential for regulatory acceptance. AI models must be comprehensively documented, robust, and reproducible to ensure reliability in regulated settings. Looking ahead, the continuous integration of AI with chromatographic instrumentation and data management systems is expected to further streamline analytical workflows. With appropriate validation and regulatory harmonization, AI is poised to become a standard supportive technology in chromatographic analysis, augmenting analytical performance while preserving the essential role of scientific judgment.

Keywords: *Artificial intelligence, chromatographic analysis, pharmaceutical quality control, regulatory compliance, AI assisted chromatography, automated data analysis, analytical validation.*

Corresponding author:

Sai Teja.B,

Department of Pharmaceutical Analysis,
Chalapathi Institute of Pharmaceutical Sciences,
Lam, Guntur, A.P, India-522034.
saitejareddy2606@gmail.com

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1. INTRODUCTION:

Artificial intelligence (AI) is specifically refers to algorithms or robots that are capable of copying and suppressing the human capabilities by perceiving and interacting with the environment. These AI techniques provide tools &methods to create intelligent systems that can learn, adapt & solve and transforming various aspects of our lives. AI has emerging a powerful tool for data analysis, drug research, development and offering advanced capabilities in pattern recognition, prediction and problem solving. It has been increasingly became an informative and transformative tool in analytical chemistry. It helps in enhancing accuracy, efficacy and various applications. It predict the complex biological and chemical data for identification of interactions, screen chemical libraries, predict toxicity, target identification, drug behavior, optimizing modelling, managing in drug designs, improving safety and efficacy. It also offers the potential for performance, improving outflows and improve powerful tools for data analysis. AI refers to systems capable of perceiving and interacting with environments to perform tasks typically requiring human intelligence. It includes algorithms that can learn, adapt, and solve complex problems. In analytical chemistry, AI has emerged as a transformative tool, particularly in drug research, toxicity prediction, target identification, method optimization, and performance enhancement in chromatographic workflows. [1,2]

COMMON AI TECHNIQUES USED:~

There are many types, mainly key branches of artificial intelligence are;

A) Machine learning
B) Deep learning
C) Natural language processing

MACHINE LEARNING;

Machine learning mainly focuses on the specifically building algorithms and that learn from the data and make predictions without explicit the programming. It improves method development, enhance accuracy, manage complex and high dimensional chromatographic data and to predict the optimal conditions of separation conditions in chromatography it mainly includes in the column selection, mobile and stationary phase gradient profiles, data analysis, pattern recognition, data fusion, sample analysis, feature tracking, real-time monitoring and helps in precise compound separation and identification. It also encompasses with supervised and unsupervised and reinforcement learning and different types of data and analytical tasks. It is increasingly used in chromatography to improve method development, optimization, data analysis & overall efficacy. It uses supervised, unsupervised, and reinforcement learning.[3,4]

DEEP LEARNING;

Deep learning capitalize the artificial neutral networks with multiple layers to mobilize complex features and relationship from datasets. It gives adaptive solutions to the challenges like various aspects of analysis includes peak detection, retention time prediction and automation of data processing, method optimization and interpretation and processes multidimensional chromatographic data and also simulation and data augmentation[5] .This deep learning are widely used in the learning complex relationships and are often use graph-based and sequence-based representations. It using and facilitating the impurity detection and identification in mixtures by recognizing of patterns and chromatographic data. It provides and enhancing the workflow efficiency, quality control, method validation in pharmaceutical development and production[6].

NATURAL LANGUAGE PROCESSING;

Natural language processing helps in improving data efficacy and analysis. It helps to automatically interpret an extract meaningful information from unsaturated chromatographic data like clinical trail data, scientific literature and regulatory documents-these are relevant for drug development and chromatographic studies. NLP reduces manual labor, increases accuracy and optimize experimental parameters and method validation techniques. Hence, integration of natural language processing and artificial intelligence in pharmaceutical chromatography accelerates data processing, supports regulatory compliance and chromatographic data extraction and analysis workflow and improves decision making. It is mainly used to analyze the automating and characterization of chromatographic data. It also helps in peak detection, integration, compound identification and impurity detection in high dimensional chromatographic data. It automates extraction of meaningful insights from literature, regulatory documents, and clinical data relevant to chromatography. NLP supports peak detection, compound identification, and method validation, reducing manual labor (Divekar & Prasad, 2024).[7,8]

II. SUMMATION OF AI IN ANALYTICAL CHEMISTRY: Traditional impurity detection and quantification in chromatography rely heavily on manual inspection of retention times, peak shapes, and spectra. AI automates these processes, improving accuracy and reducing analyst dependency.In analytical chemistry, the identification of impurities has traditionally leaned on a combination of manual and quantitative techniques to ensure the purity, quality & safety of pharmaceuticals, chemicals and other products[9].

Manual approaches typically involve visual inspection & comparision of chromatographic data like HPLC, GC, Chromatograms. Analyst identifies impurities based on features like retention time, peak shapes & spectral characteristics, this process is often time consuming and highly depended on the analyst expertise([10]).

Conventional computational methods aim to automate parts of this processes like peak match and spectral convulsions. AI is used in data analysis by automation tasks, improving accuracy, reducing errors & increasing efficacy([11,12]).

PATERN RECOGNITION: This technique is particularly useful for identifying similarities and differences between complex mixtures & classify complex data obtained from various chemical profiles. It mainly involves using computational methods to analyze and to identify the data, patterns & relationships within the data([13,14]).

DATA ANALYSIS: This technique involves the using of machine learning algorithms and advanced algorithms to analyze the historical data and automatically identify patterns, insights from the chromatography data with reduced errors and to handle complex databases. This also includes the quantification and method development. AI enhances the data analyses by providing accuracy and speed([15,16]).

DATA FUSION: Data fusion combine with AI enhances the data explanation by merging information from several sources and techniques. Data fusion enables more accurate, efficient and automated methods. AI algorithms can provide a more wide-ranging & stable complex samples.(17,18)

SAMPLE ANALYSIS: Sample analysis of a chromatographic technique using AI tools like machine learning& data visualization. Its main objective is to analyze HPLC. AI algorithms can predict optimal separation, analyze data, patterns for efficient analysis.[19]

COLUMN SELECTION: AI algorithms use column type, mobile& stationary phases and parameters and analyze datasets to predict optimum column type. It can predict column performances by based on factors like column length and diameter leads to optimum separation, Thus helps in faster method development.[20]

SCREENING CHEMICAL LIBRARIES: This mainly used in AI tools for the growing field of drug discovery, analytical chemistry, improving accuracy & for data processing. Its main objective is to enhance the speed and efficacy to recognize bioactive or target-specific compounds from chemical libraries by initiating with AI.[21]

PREDICT TOXICITYS: The main objective to predict toxicity of chemical compounds by integratinchromatography data with AI models, it detects the site at early stage of harmful substances in chemical libraries. It mainly works by data collection, extraction, integration with database & toxicity prediction using AI. It analyses the datasets & identifying patterns in traditional methods may miss[22,23]

DRUG BEHAVIOUR: The main objective is to analyze and predict how a drug behaves in chemical systems (ADME).(24).AI algorithms can predict optimized chromatographic methods, drug properties & to identify patterns. It leads to development and manufacturing processes(25).

TARGET IDENTIFICATION: The main objective is to identify biological target of a specific enzyme or receptors of targets to be detected. It enhances the accuracy and automation in data processing. It is a process to discover the biological molecule to interact with the drug. AI algorithm identify the peaks and predict compound properties & more reliable target identification([26,27,28]).

OPTIMIZE MODELLING: The main objective is to improve the accuracy, performance& transparency of AI models([29]). It can predict optimal separation of parameters & control the process in real time, enhance the sensitivity([30]).

AUTOMATION OF DATA PROCESSING: It mainly helps to enhance the accuracy & improving efficiency. The AI tool can significantly streamline workflows reduce human error. The AI transform the chromatography from a manual, labor intensive process to a more efficient[31-33].

METHOD OPTIMIZATION: Basically the process involves to enhance the accuracy and enabling automation[34]. Method optimization in chromatography involves the several experimental queries to achieve better resolution & greater sensitivity. AI tool has significantly enhance the optimization process([35]).

INTERPRETATION OF DATA: The data interpretation is done by automating and enhancing the AI algorithms to detect the accuracy, peak identification and optimatization.it is enabling accurate and more robust analysis of chromatographic samples([36,37]).

PROCESSING OF DATA: It mainly works by enhancing automation, precision and efficacy. It also involves interpreting raw signals to quantify,

validate & identify compounds. Basically, this process from ancient times involves manual steps when, AI has introduced it starts to improve every stage from peak detection to reporting[38-40].

COMPOUND IDENTIFICATION: In current chromatography, mainly combined with mass spectroscopy, compound identification is a complex step[41]. AI algorithm is significantly used to analyze complex data, to identify peaks and to predict compound properties[42,43].

METHOD VALIDATION: AI tools are increasingly used to enhance, accelerate method validation in chromatographic techniques. It ensures that the analytical method is reliable, reproducible and suitable for intended purpose[44,45,47].

IMPURITY DETECTION: It is a crucial step in pharmaceutical analysis, environmental testing, food safety, these AI mainly approaches to enhance automation in identifying impurities([48.50].

Table-1. AI in Chromatography

Chromatographic technique	Manual method	AI method
Gas chromatography	• requires trial and error to optimize method development • it has limited automation.[4] • Detectors used: electron capture detector, nitrogen-phosphorous detector. Etc..	• It can analyze data to predict optimal conditions for faster • It has greater automation in all aspects[5] • Soft wares used: Agilent Mass Hunter, open chrom.
Paper chromatography	• The sample spots are applied manually to the chromatography paper by using capillary tubes etc. • It requires visual inspection of the chromatogram([6]. • Detectors used: spraying agents (ninhydrin, FeCl3, I2 vapor), specific reagents (based on functional groups), uv-vis detectors. Etc…	• The sample spots are applied by AI enhanced robotic system and AI algorithms. • It can be integrated with chromatographic system to automatically acquire data for further analysis of chromatograms.[13] • Soft wares used: image J + AI Plugins, YOLO.
High performance thin layer chromatography	• It involves manual placing of TLC plate in a chamber • It involves manual measurement and calculations of Rf values and peak areas. • Detectors used: densitometers, absorbance detectors[19], charged aerosols detectors. Etc…	• Solvent selection is used for efficient separation • Potentially increases the accuracy and speed than manual method[21]. • Soft wares used: CAMAG Vision CATS, ImageJ.
High performance liquid chromatography	• It is a time-consuming process and requires expensive experimentation. • The sample is injected manually by using syringes[21] • Detectors used: evaporative light scattering detectors, UV-VIS detectors, refractive	• It can accelerate method development by predicting optimal conditions. • The sample is injected by utilizing automated autosamplers[31]. • Soft wares used: Agilent, open lab CDS, cerno bioscience-mass works.

	index detectors. Etc..	
Thin layer chromatography	• It requires manual measurement of spot distances • It involves physically spotting samples on to a TLC plate[32] • Detectors used: fluorescence detectors, UV detectors. Etc..	• This process involves insertion of images in TLC plate. • It employs image analysis n& machine learning to employ spots[34] • Soft wares used: Image J, CNN based AI models.
Liquid chromatography	• It requires significant time & expertise to manually optimize conditions. • Manual peak integration is tedious & potentially inaccurate • Detectors used: UV-VIS absorbance detectors[38], fluorescence detectors. Etc..	• It can analyze large datasets to predict optimum conditions • It reduces analysis time by automating several steps[42]. • Soft wares used: Open lab, CDS, Deep LC.
Column chromatography	• it requires careful manual execution of each step including packing the column and collecting fractions. • it involves visual inspections of fractions, manual integration of peaks[32] • Detectors used: mass spectrometers, fame ionization detectors, uv detectors. Etc.	• AI driven systems can automate the entire process from sample injection to data analysis. • It can automatically analyze data and identify peaks[22]. • Soft wares used: Biotage, seleckt, BUCHI Pure.
Ion exchange chromatography	• It requires manual adjustment of parameter like pH, ionic strength • Manual handling increases the risk of human errors in sample preparations[20]. • Detectors used: conductivity detectors, electrochemical detectors, RI, UV-VIS, fluorescence detectors. etc…	• It can analyze experimental data and predict optimal parameters. • AI can minimize the human errors and inconsistencies, leads to accurate data[15]. • Soft wares used: Cytiva UNICORN, Biopharma finder.
Affinity chromatography	• It requires direct manipulation of the column & buffers. • It is a time-consuming process especially for large sample cells. • Detectors used: UV-VIS absorbance detectors[16], mass spectrometer detectors, fluorescence detectors, RI detectors.	• It analyses the data from previous runs, predict optimal conditions. • It significantly speeds up the process[12]. • Soft wares used: UNICORN, Chromeleon.

	Etc..	
Size exclusion chromatography	• It involves manually injecting samples and analyze them using detectors like UV- vision. • Due to human error it may not achieve optimal resolution[69]. • Detectors used: light scattering detectors, UV-VIS detectors, RI detectors. Etc..	• AI can integrate with online detectors and automated fraction, collection, automated sample preparation. • It significantly improves resolution, reduce analysis time & shorten human intervention[67]. • Soft wares used: custom AI, waters, empower-3.

III. APPLICATIONS OF AI IN CHROMATOGRAPHIC WORKFLOW:

3.1 PEAK DETECTION & DECONVOLUTION:

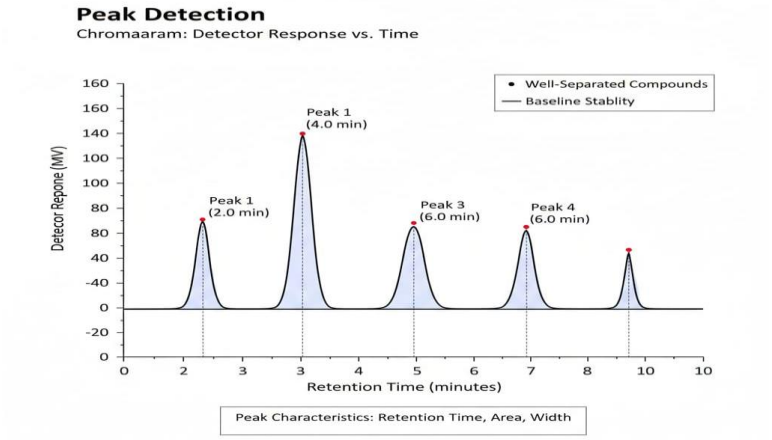
-peak detection; A peak in a chromatogram represents a compound separating from a column and these are detected by the detectors[51]. Peaks can be identified by retention time, peak area& peak width. The common software used for peak detection is "*chem station, open chrom& phyton libraries.*

-Deconvolutions; it is a mathematical process of resolving, overlapping peaks in a chromatogram to characterize and quantify a individual components[53]. Due to deprivation of deconvolution leads to A) overlapping peaks are not separated.

B) it purifies the compounds may appear as single peak.

C) data interpretation becomes less reliable.

The common software used for deconvolution is "*AMDIS, XC-MS& Mass Hunter* [55].



-01: *Peak detection and deconvolution enable precise resolution of overlapping chromatographic signals, ensuring accurate quantification.*

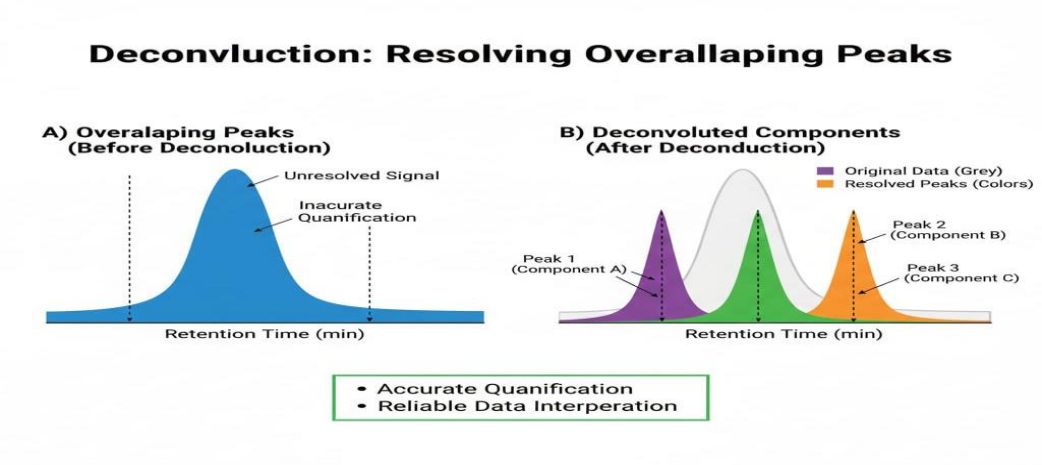


Fig:2- These processes strengthen data reliability and support robust interpretation of complex analytical profiles.

3.2RETENTION TIME PREDICTION: predicting retention time is crucial for recognize compounds, enhancing methods & automating work flows in chromatography[56]. It works by quantitative structure retention relationship, rule-based models, data bases.

It helps by speeds up the method development, improves compound annotation in untargeted analyses. The common software used for retention time prediction is "*pred Ret, Auto RT,DeepRT*[52,54,57,58].

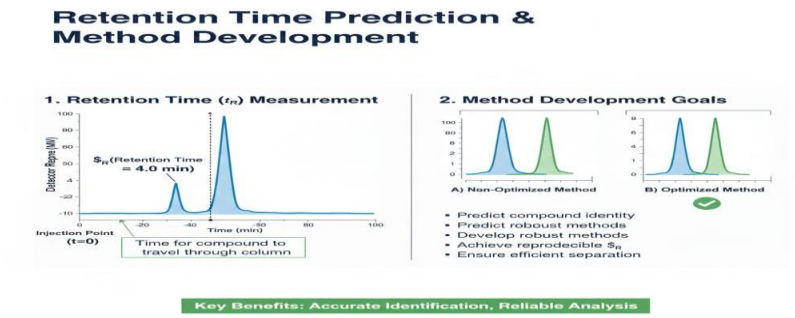


Fig 3(a):Retention time prediction supports rational chromatographic method development and optimized peak separation.

Fig 3:Accurate [t_R] measurement enables reliable identification, reproducible retention times, and robust quantitative analysis.

3.3METHOD DEVELOPMENT: Chromatographic method development involves designing& refining a eluting process to accurately & reliably analyze compounds in a mixture[59].

It is mainly used for A) efficient separation of components
B) reproducible retention times
C) Accurate quantification

The most commonly used software used for *"chromeleon CDS, Empower, Dry lab, Apex Track.*

3.4QUANTIFICATION & CALIBRATION:

Quantification; It helps to determine the absorption (or) amount of an analyte in a sample using the peak area/ peak height in the chromatogram.

It can be works by many methods like

A. External standard method
B. Standard addition method
C. Normalization method

The most commonly used software in quantification is *Empower, BGC-Argo AI, Scie X OS software*.

Calibration; It is process of initiating a relationship between the equipment response and known concentration of analyte. It allows for enumeration of unknown samples[60].

It helps to

A. Ensures accurate & reliable quantification
B. Verifies linearity, perception
C. Required for regulatory co-operation.

The most commonly used software in calibration is BLOOM, Mass Hunter, chemometric soft wares.

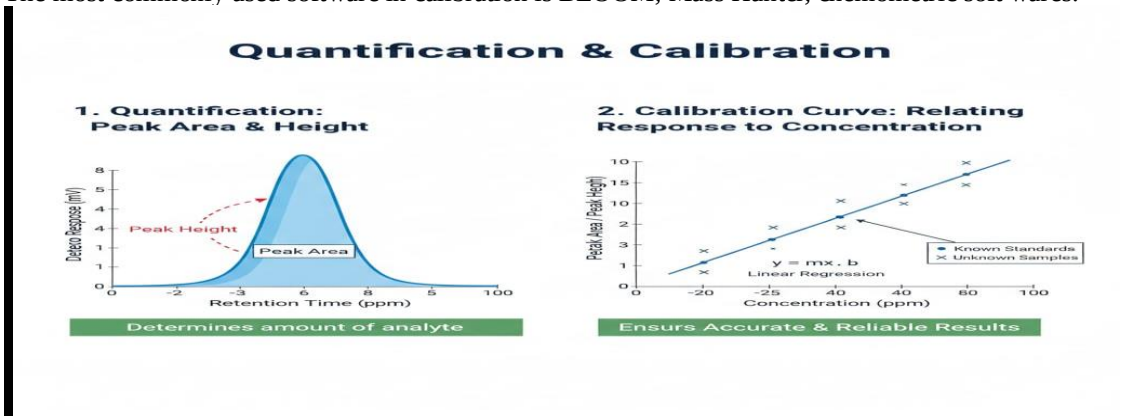


Fig 4:Quantification and calibration link chromatographic peak response to analyte concentration, ensuring linearity and regulatory-compliant accuracy.

Fig 4(b):Integrated with data mining and fault detection, these tools transform raw chromatographic output into reliable, decision-ready information.

3.5DATA MINING: It involves retrieving meaningful patterns, trends& relationship from complex chromatographic datasets using analytical, machine learning tools.

Data mining is applied in chromatography

A. Metabolomics
B. Food& plant analysis
C. Pharmaceutical quality assurance.

The most commonly used software in data mining is MZ mine 3, XCMS, SIMCA**(61)**.

3.6 FAULT DETECTION: It refers to detect problems (or) deviations during chromatographic analysis that can embody data quality, instruments performance (or) chain of custody.

It helps to forestall sample loss, mitigate downtime due to system failure.

The common soft wares used for fault detection is ACD, Sci Cord ELN+CDS, KNIME +Custom models**(62)**,

IV. CASE STUDIES & REAL-WORLD IMPLEMENTATIONS:

1. Protein A Chromatography with ML for Anomaly Detection and Yield Prediction

Researchers applied advanced ML—including PCA + Isolation Forest and LSTM autoencoders—to detect column integrity issues in protein A capture chromatography up to 4 cycles ahead. Additionally, a hybrid PLS-ANN model achieved strong yield prediction ($R^2 \approx 0.96$, RMSE ≈ 0.014), outperforming traditional PLS ($R^2 \approx 0.88$, RMSE ≈ 0.028). This supports real-time control in continuous biomanufacturing.

2. Automated TLC with ML for R_n Prediction (Thin-Layer Chromatography)

An automated, high-throughput TLC platform collected nearly 5,000 R_n values from 387 compounds under varied solvent conditions. ML models were then trained to accurately predict R_n curves, aiding solvent selection and expediting chromatographic separation planning.

A related study using CAMAG's complementary developing solvents approach tested regressors (random forest, SVM, linear regression). Random Forest delivered R^2 values of ~0.87 and ~0.71 for different conditions, with prediction errors under 0.1 in many cases[63].

3. HPTLC Using ML in High-Performance Thin-Layer Chromatography

High-throughput HPTLC combined with non-targeted screening allowed ML regressors to predict R_n values for reference substances. The models' effectiveness varied based on training/test set similarity, underlining the importance of data representativeness[64].

4. Data-Driven Models for Chromatographic Purification

In a review of the field, predictive ML models—including multiple linear regression (MLR), SVM, and ANN—were used for:

- Modeling herbal extract separation conditions ($r > 0.99$)
- Linking synthetic nucleotide properties to retention times (SVR: R^2, $Q^2 > 0.99$, vs. empirical logarithmic models at $R^2 \sim 0.93$, $Q^2 \sim 0.85$)
- Modelling antibody purification, HCP elution, and peak detection tasks[65].

5. Machine Learning for Column Performance Prediction

ML models were trained to predict chromatographic performance characteristics—like reduced plate height (h) and peak asymmetry (A_s)—based on column attributes such as dimension, particle size, and packing material. This offers an alternative to pure theoretical rate models by revealing empirical relations between manufacturing variables and performance[66].

6. Deep Learning for Retention Time Prediction (RT)

- DeepRT (Proteomics): A deep CNN + RNN model predicts peptide RT in LC-MS, outperforming previous methods like ELUDE and GPTime.
- Quantile Geometry-enhanced GNN for Enantioseparation: Uses graph neural networks and structural data to predict retention times of chiral molecules in HPLC, enabling estimation of separation probabilities.
- ChromAlignNet for GC-MS Alignment: A deep learning model aligns GC-MS peaks across samples without user-specified reference chromatograms and shows excellent AUC performance.
- "Intelligent Chemical Purification" (2024): An ML approach with transfer learning predicts key chromatography parameters and defines a novel "separation probability" metric, demonstrating scalable AI-augmented purification[67].

7. Metabolomics—Retention Time Prediction for Small Molecules

ML tools have been developed to predict retention times of small molecules in complex matrices like plasma or plant extracts, improving identification and interpretation in metabolomics workflows.

8. Golm Metabolome Database (GC-MS via Decision Trees)

The Golm Metabolome Database employs decision trees to classify substructures in GC-MS data and transfer retention index (RI) information across chromatography variants—using structural feature extraction as training inputs(68).

V. BENEFITS OF AI IN CHROMATOGRAPHIC TECHNIQUES:

there are some innovative & less commonly analyzed benefits of applying AI in chromatographic techniques:

- PREDICTIVE MAINTANANCE
- AUTOMATED DATA ANALYSIS
- ADVANCED ERROR DETECTION& CORRECTION
- HYPERSPECTRAL IMAGING INTEGRATION
- REAL TIME ADAPTIVE PARAMETER CONTROL
- ENHANCED DATA INTERPRETATION
- FASTER METHOD DEVELOPMENT
- ENHANCED RESEARCH & DEVELOPMENT
- INCREASED EFFICACY &REPRODUCABILITY

VI. REGULATIONS OF AI IN CHNROMATOGRAPHIC TECHNIQUES:

- DATA QUALITY & CONSISTENCY
- IT NEEDS HIGH- QUALITY DATA SETS
- LACK OF STANDARDISATION
- POTENTIAL AUTOMATION ERRORS
- POOR GENERALIZATION
- REGUALATORY UNCERTAINITY
- RISK OF UNINTENDED CONSEQUENCES
- HUMAN- COMPUTER ERRORS

VII.FUTURE PERSPECTIVES:

Green and sustainable chromatography
Integration with multi-omics and systems biology
Regulatory compliance
Real-time monitoring and adaptive control
Smart chromatography systems

CONCLUSION:

Artificial intelligence has swiftly transitioned from a conceptual frontier to a foundational force in analytical chemistry. Its integration into chromatographic workflows and chemical data interpretation is not merely a technological upgrade—it represents a paradigm shift in how scientists engage with complexity, precision, and scale. By leveraging machine learning, deep learning, and natural language processing, AI now automates tasks such as peak detection, retention time prediction, impurity profiling, and method development—processes that previously relied on manual expertise and were prone to variability[69].This transformation is not just about accelerating throughput or reducing labor; it's about enhancing the integrity and depth of scientific inquiry. AI improves reproducibility, minimizes human bias, and enables faster, more informed decision-making. Researchers are increasingly able to redirect their focus from routine data handling to strategic problem solving and hypothesis generation[70]. In pharmaceutical sciences, AI facilitates drug discovery by predicting molecular interactions, screening vast chemical libraries, and optimizing safety and efficacy profiles[71]. In metabolomics, food safety, and environmental analysis, AI empowers high-throughput, multidimensional data processing, revealing subtle patterns and correlations that traditional methods often miss. AI's role particularly compelling is its ability to transform data abundance into actionable insight. Analytical chemistry today generates massive volumes of complex data, and AI serves as the interpretive engine that extracts meaning, guides experimentation, and informs regulatory and industrial decisions[72,74]. It bridges the gap between raw information and scientific understanding, turning data into knowledge—and knowledge into innovation[73].AI is revolutionizing chromatography by improving speed, accuracy, reproducibility, and sustainability[75]. Integration of machine learning, deep learning, and NLP enables automation in peak detection, retention prediction, method development, and impurity detection. Real-world applications in pharmaceuticals, metabolomics, food, and environmental analysis demonstrate AI's transformative potential in analytical chemistry.

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