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"Advanced Modern NMR Techniques Enhance the Efficacy of Pharmaceutical Analysis"

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ABSTRACT
Nuclear magnetic resonance (NMR) spectroscopy has become an indispensable tool in pharmaceutical analysis, providing crucial insights into the structure, dynamics, and interactions of drug molecules. Advancements in NMR instrumentation, pulse sequences, and data analysis methods have significantly enhanced its capabilities, enabling more efficient and effective analysis. This review explores these advanced techniques, including multidimensional NMR, solid-state NMR, quantitative NMR (qNMR), diffusion-ordered spectroscopy, and hyphenated techniques like LC-NMR and LC-MS-NMR. We discuss their applications in drug discovery, development, and quality control, highlighting their impact on pharmaceutical research. These techniques provide detailed structural information, enable the characterization of complex mixtures, and facilitate quantitative analysis, ultimately leading to the development of safer and more effective pharmaceutical products.

Key words : Nuclear Magnetic Resonance (NMR) Spectroscopy, Multidimensional NMR, Solid-state NMR, quantitative NMR (qNMR), Diffusion-ordered spectroscopy, Hyphenated techniques.

I. INTRODUCTION

Shortly after World War II, nuclear magnetic resonance (NMR) spectroscopy was developed.

The most potent analytical technique is nuclear magnetic resonance (NMR) spectroscopy. It makes it possible to see individual atoms and molecules in a variety of media, both in their solid and solution states. Non-destructive NMR provides a molar response that enables simultaneous structure elucidation and quantification. Spin-spin ("J-") couplings are produced by magnetic interactions between NMR-active nuclei along covalent bonds. The nuclear Overhauser effect (NOE) can be used to identify through-space interactions. Clarification of the three-dimensional structure is made possible by both interactions.

Nuclear Magnetic Resonance spectroscopy has become a cornerstone analytical technique in the pharmaceutical industry, offering a unique blend of qualitative and quantitative capabilities for analyzing a wide range of molecules, from small organic compounds to complex biopharmaceuticals[1].

The list of Noble Prize recipients demonstrates the consistent advancement in NMR spectroscopy. Rabi received the first Nobel Prize in physics in 1944 for creating a resonance technique that makes it possible to record the magnetic characteristics of atomic nuclei. Due to their independent work on the first practical NMR experiments in 1945 at various locations, Bloch and Purcell were awarded the prize in 1952. By that point, NMR spectroscopy had evolved beyond a simple physical experiment. Since the "chemical shift" was discovered, the technique has been used by chemists to clarify structures. Continuous wave (CW) (NMR) spectrometers were the first practical devices that used electromagnets. Their utility came to an end with the upcoming superconductor magnets in the 1970s. However, only since Emst developed the basics of the Fourier transformation (FT) method, the foundation of the modern NMR spectroscopy methods was laid. Since NMR spectroscopy was by then a domain of physicians, Emst was the first chemist in the list of Nobel Prize winner in 1991. A decade later, Wiithrich was the second honoured chemist He received the Prize in 2002 for the elucidation of three-dimensional structures of macromolecules. The NMR technique has become an important tool in other scientific fields, especially in medicine[2].

FIG 1: NMR SPECTROSCOPY

FUNDAMENTAL PRINCIPLE OF NMR SPECTROSCOPY

NMR spectroscopy hinges on the magnetic properties of atomic nuclei. Nuclei with an odd number of protons or neutrons possess an intrinsic angular momentum called spin, which generates a small magnetic moment. When placed in a strong external magnetic field (B0), these nuclear spins align either with or against the field, creating two energy levels. The lower energy state corresponds to alignment with B0, while the higher energy state corresponds to alignment against B0.

The energy difference between these two states is proportional to the strength of the magnetic field and the gyromagnetic ratio (γ) of the nucleus, a constant specific to each isotope:

$\Delta E = \gamma\hbar B_0$

where ħ is the reduced Planck constant.

When a radiofrequency pulse with energy equal to ΔE is applied to the sample, nuclei in the lower energy state can absorb this energy and transition to the higher energy state. This absorption of energy is known as **resonance.** The frequency of the RF pulse required for resonance, known as the Larmor frequency (ν0), is also proportional to the magnetic field strength and gyromagnetic ratio:

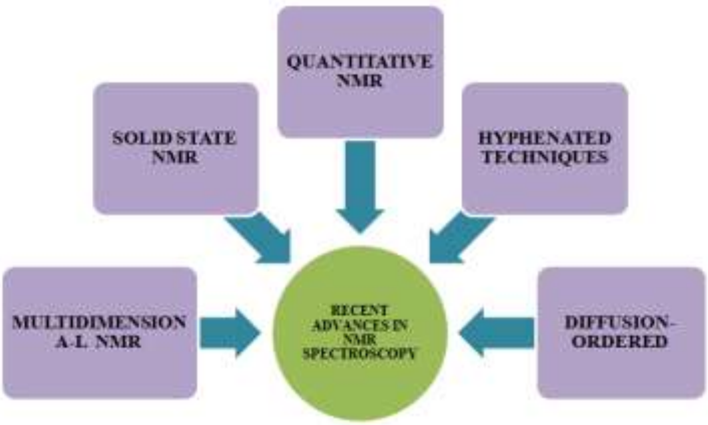
$\nu_0 = \frac{\gamma B_0}{2\pi}$

After absorbing the RF energy, the excited nuclei return to their lower energy state through a process called **relaxation**. The emitted energy during relaxation is detected and processed to generate an NMR spectrum[3].

The precise resonance frequency of a nucleus is influenced by its local electronic environment, a phenomenon known as **chemical shift**. Electrons surrounding a nucleus shield it from the external magnetic field, altering the effective magnetic field experienced by the nucleus. This shielding effect causes nuclei in different chemical environments to resonate at slightly different frequencies, providing valuable information about the molecular structure.

RECENT ADVANCES IN NMR SPECTROSCOPY

Recent advances in NMR spectroscopy analysis include: increased sensitivity through improved instrumentation, the integration of artificial intelligence for data analysis, the use of advanced pulse sequences for complex molecular systems, the application of solid-state NMR for studying solid materials, and the development of techniques for real-time monitoring of metabolic processes; particularly highlighting its use in metabolomics, where NMR can be used to identify and quantify small molecules within a biological sample, allowing for a deeper understanding of metabolic pathways[4].



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MULTIDIMENSIONAL NUCLEAR MAGNETIC RESONANCE (NMR) SPECTROSCOPY

Multidimensional Nuclear Magnetic Resonance (NMR) spectroscopy has long been a cornerstone of pharmaceutical analysis, offering valuable insights into the structure, composition, and dynamics of pharmaceutical compounds. Over the past few decades, significant advances in multidimensional NMR techniques have expanded their capabilities, enabling deeper and more comprehensive analysis of complex drug molecules and formulations. This review highlights recent developments in multidimensional NMR in the context of pharmaceutical analysis, focusing on its applications in drug discovery, quality control, and formulation development.

1) Advances in NMR Techniques for Pharmaceutical Analysis

Multidimensional NMR techniques have significantly advanced the role of NMR in pharmaceutical analysis, enabling detailed studies of drug candidates' molecular structure, conformation, interactions, stability, and purity.

- **2D NMR**: Techniques like COSY, HSQC, and TOCSY are essential for determining atom connectivity and correlations. These are particularly useful for elucidating structures of small molecules and complex drug candidates, resolving overlapping signals from nuclei like ^1H and ^13C.
- **3D & 4D NMR**: For larger drug molecules such as biologics and peptides, 3D and 4D NMR (e.g., 3D-TOCSY, 3D-NOESY, 4D-HSQC) enhance spectral resolution and help study interactions and dynamics of large biomolecules.
- **Cryogenic NMR**: Cryogenic probes improve sensitivity and resolution by operating at lower temperatures, enabling the detection of low-concentration drug candidates and impurities, crucial for drug development and quality control.
- **Time-Resolved NMR**: This technique tracks dynamic processes, such as drug-target interactions, binding kinetics, and degradation, providing insights into drug stability and metabolite formation[5].

2) Applications in Drug Discovery and Development

Multidimensional NMR is crucial in the discovery, development, and optimization of pharmaceutical compounds, providing key insights into molecular interactions, structure, and drug efficacy.

- **Structural Elucidation**: Multidimensional NMR enables complete structural determination of novel drug candidates, confirming identity and purity, particularly for complex molecules or natural products.
- **Protein-Ligand Interactions**: Techniques like 2D-^1H-^15N HSQC and 3D-NOESY are used to study drug-protein interactions, identify binding sites, and understand conformational changes. This aids in optimizing drug efficacy and designing selective drugs. NMR also helps in determining binding kinetics and dissociation constants (K_d).
- **Metabolite Profiling**: NMR aids in studying drug metabolism by identifying and quantifying metabolites, crucial for understanding metabolic pathways, drug-drug interactions, and toxic metabolites.
- **High-Throughput Screening (HTS)**: Multidimensional NMR is used for screening compound libraries in complex mixtures to identify lead compounds based on target interactions, without labeled reagents[6].

3) Applications in Pharmaceutical Formulation and Quality Control

Multidimensional NMR provides distinct advantages over traditional methods like chromatography and mass spectrometry, offering detailed structural insights and the ability to monitor complex mixtures in solution.

- **Drug Purity Assessment**: NMR detects impurities, including residual solvents, excipients, and degradation products, using techniques like 2D-^1H-^13C HSQC to assess the purity of small molecules and biologics.
- **Stability Studies**: NMR monitors drug stability over time by detecting chemical changes, degradation products, or conformational shifts, aiding in shelf-life testing and formulation development.
- **Polymorphism and Solid-State NMR**: Solid-state NMR identifies polymorphs and examines the stability of different drug crystal forms, affecting solubility, bioavailability, and efficacy.
- **Drug-Excipient Interactions**: Multidimensional NMR analyzes interactions between drugs and excipients, helping

optimize formulations for improved stability and drug release.

4) **Challenges and Future Directions**

- **Sensitivity and Sample Size**: NMR is less sensitive than techniques like mass spectrometry, especially for low-concentration samples. Advances in cryogenic probes and sensitive isotopes (e.g., ^13C, ^15N) are improving sensitivity.
- **Complex Data Interpretation**: Multidimensional NMR generates large datasets, which can be difficult to analyze, particularly for large biomolecules. Automated software and machine learning are helping, but manual analysis is still time-consuming for complex systems.
- **Cost and Accessibility**: High-field NMR and cryogenic probes are expensive, limiting access for smaller labs. However, more affordable benchtop NMR spectrometers are improving accessibility for routine analysis[7].

➢ **SOLID-STATE NUCLEAR MAGNETIC RESONANCE (SS-NMR) SPECTROSCOPY**

Solid-state Nuclear Magnetic Resonance (SS-NMR) spectroscopy has emerged as a powerful technique for the analysis of pharmaceuticals, especially in the context of solid forms like powders, tablets, and crystalline structures. Unlike solution-state NMR, which requires samples to be in liquid form, SS-NMR allows for the study of solid compounds without the need for complex sample preparation. Recent advances in SS-NMR techniques have greatly expanded its application in pharmaceutical analysis, enabling more detailed structural, morphological, and dynamical studies of drugs and their formulations. This review provides an overview of recent developments in SS-NMR and its growing role in pharmaceutical research, focusing on applications in drug discovery, formulation development, quality control, and stability testing[8].

1. Applications of Solid-State NMR in Pharmaceutical Analysis

1.1 Structural Characterization of Drug Polymorphs with SS-NMR

- **Identification and Differentiation of Polymorphs**: SS-NMR, especially with MAS, provides detailed insights into molecular packing and intermolecular interactions in crystalline solids, enabling the differentiation of polymorphs based on subtle chemical environment differences in nuclei (e.g., ^13C, ^15N).
- **Polymorph Screening**: High-throughput SS-NMR facilitates rapid screening of crystalline samples, helping identify new polymorphs early in drug development and optimize properties like solubility and stability.

1.2 Drug-Excipient Interactions with SS-NMR

- **Drug-Excipient Compatibility**: SS-NMR, especially 2D-^1H-^13C correlation spectroscopy, helps study molecular-level interactions between drugs and excipients, providing insights into their impact on solubility, release, and stability.
- **Detection of Amorphous Forms**: SS-NMR identifies amorphous drug forms, which are more soluble but less stable than crystalline forms. Their presence can affect drug dissolution rates and long-term stability.

1.3 Study of Solid-State Drug Degradation and Stability

- **Stability Studies**: SS-NMR tracks chemical changes in drugs over time during stability testing, detecting degradation products or structural changes, such as isomer or hydrate formation, to assess long-term stability.
- **Polymorphic Transitions**: SS-NMR monitors polymorph transformations, providing critical data on the conditions under which these transitions occur, ensuring the drug remains in its desired form during its shelf life.

1.4 Characterization of Drug Solubility and Bioavailability

- **Crystallinity and Solubility**: SS-NMR directly assesses the degree of crystallinity and amorphous content in drugs. Amorphous forms typically have higher solubility, enhancing bioavailability. SS-NMR helps differentiate between crystalline and amorphous forms to optimize drug formulation for better solubility and bioavailability.

1.5 Monitoring Solid-State Drug Delivery Systems

- **Lipid-Based Drug Delivery**: SS-NMR provides detailed structural information about lipid formulations (e.g., liposomes, solid lipid nanoparticles) used in drug delivery. It helps analyze drug-lipid interactions, optimizing controlled-release systems and enhancing therapeutic efficacy[9].

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2. Challenges and Future Directions

- **Sensitivity**: SS-NMR remains less sensitive than solution-state NMR or mass spectrometry, making it difficult to analyze low-concentration samples or complex formulations, despite advances like Dynamic Nuclear Polarization (DNP).
- **Complexity of Data Interpretation**: SS-NMR spectra can be complex, especially for heterogeneous samples or multi-component systems, requiring specialized expertise in both NMR and pharmaceutical sciences.
- **Cost and Accessibility**: High-field NMR instruments and techniques like DNP are costly, limiting access for smaller companies or research labs. However, advancements in benchtop NMR instruments may improve accessibility in the future.

➢ QUANTITATIVE NUCLEAR MAGNETIC RESONANCE (QNMR) SPECTROSCOPY

Quantitative Nuclear Magnetic Resonance (qNMR) spectroscopy has emerged as a powerful and reliable analytical technique in pharmaceutical analysis, offering advantages over traditional methods such as chromatography and mass spectrometry. Unlike other techniques, qNMR provides direct, non-destructive measurements of compound concentration without the need for calibration curves, complex sample preparation, or reference standards in many cases. Over recent years, significant advancements in qNMR methods have made it increasingly valuable in pharmaceutical research, formulation, quality control, and stability testing. This review explores the recent developments in qNMR and its growing role in pharmaceutical analysis.

1) **Technological Advancements in Quantitative NMR (qNMR)**

- **Higher-Field NMR Instruments**: Enhanced sensitivity and resolution with 500 MHz, 600 MHz, and 800 MHz spectrometers improve analysis of complex samples, enabling precise quantification at low concentrations.
- **Advanced Pulse Sequences**: New sequences improve accuracy by reducing noise and enhancing signal-to-noise ratios, especially for low-concentration compounds.
- **Cryogenic Probes**: Increased sensitivity via cryogenic probes allows for quantification of trace impurities and active pharmaceutical ingredients (APIs) in complex mixtures.
- **Automated and High-Throughput qNMR**: Automation and software platforms enable more efficient routine analysis, reducing time and resources for batch processing[9].

2) Applications in Pharmaceutical Analysis

- **Quantification of APIs**: qNMR offers precise quantification without the need for calibration standards, using single-peak or internal standard methods for accurate measurements.
- **Drug Formulation and Excipients Analysis**: Simultaneous quantification of APIs and excipients in complex formulations, aiding in ensuring proper composition and avoiding unintended interactions.
- **Impurity Detection**: qNMR enables the identification and quantification of impurities, enhancing quality control and shelf-life studies.
- **Polymorphism Studies**: qNMR can quantify different polymorphs of a drug, which affect solubility, bioavailability, and stability, ensuring drug consistency.
- **Stability and Shelf Life Testing**: qNMR is useful for monitoring drug stability over time, identifying degradation products and optimizing storage conditions.

3) Challenges and Future Directions

- **Sensitivity**: qNMR remains less sensitive than HPLC or mass spectrometry, especially for low-concentration compounds.
- **Complex Mixtures**: Signal overlap in complex formulations can hinder accurate quantification, but advancements in pulse sequences and software are helping overcome this.
- **Cost and Accessibility**: High-field NMR spectrometers and cryogenic probes are expensive, though benchtop NMR systems are improving accessibility.
- **Standardization**: The lack of universal protocols for qNMR limits its widespread adoption; standardization efforts will improve reliability and reproducibility[10].

➢ DIFFUSION-ORDERED NUCLEAR MAGNETIC RESONANCE (DOSY) SPECTROSCOPY

Diffusion-Ordered Nuclear Magnetic Resonance (DOSY) spectroscopy has emerged as an increasingly valuable analytical tool in pharmaceutical analysis. This technique provides insights into the molecular size, shape, and dynamics of chemical species in solution by measuring the self-diffusion coefficients of different components. DOSY can resolve complex mixtures, quantify molecular interactions, and reveal structural information about pharmaceutical compounds, all without the need for separation or labeling. Over the past decade, significant advancements in DOSY-NMR technology have enhanced its sensitivity, resolution, and applicability, making it an essential tool for pharmaceutical researchers. This review explores the recent developments in DOSY-NMR and its growing role in the analysis of pharmaceutical compounds and formulations[11].

1. Principles and Advancements in DOSY-NMR

DOSY-NMR measures molecular diffusion in solution, using gradient pulses to separate signals based on diffusion coefficients. Larger molecules diffuse slower than smaller ones, allowing size and shape analysis. Recent advancements in DOSY-NMR have improved its sensitivity, precision, and utility, making it a more versatile tool for pharmaceutical analysis.

- **Improved Sensitivity and Resolution**: Higher-field NMR spectrometers (e.g., 600 MHz, 800 MHz) and advanced gradients enhance resolution, especially for large molecules like proteins or polymers.
- **High-Resolution DOSY**: Optimized gradients and pulse sequences improve the separation of overlapping species in mixtures
- **Time-Resolved DOSY**: Tracks diffusion over time to monitor dynamic processes like drug binding or formulation changes.
- **Multidimensional DOSY**: Combines with 2D/3D NMR for more detailed molecular interaction and structural information.

2. Applications of DOSY-NMR in Pharmaceutical Analysis

2.1 Characterization of Pharmaceutical Formulations

- **Component Identification**: Separates and quantifies components in complex formulations (e.g., API and excipients).
- **Stability Monitoring**: Tracks diffusion coefficient changes to detect degradation or aggregation in formulations.
- **Quantification**: Provides a holistic view of formulation composition by quantifying drugs and excipients simultaneously.

2.2 Studying Drug Release Profiles

- **Polymer Systems**: Studies diffusion of drugs through polymer matrices in controlled-release formulations.
- **Quantitative Release Analysis**: Measures diffusion changes to analyze drug release kinetics for sustained-release formulations.

3. Challenges and Future Directions

- **Sensitivity**: Requires relatively high concentrations of analytes, limiting its use for low-concentration samples or complex mixtures.
- **Data Analysis**: Analyzing complex mixtures or overlapping diffusion coefficients remains challenging; further development of computational tools is needed.
- **Time-Resolution**: Long acquisition times limit real-time applications; improvements in acquisition speed and NMR instrumentation are needed[12].

➢ HYPHENATED NUCLEAR MAGNETIC RESONANCE (NMR) SPECTROSCOPY

Hyphenated techniques, such as **LC-NMR (Liquid Chromatography-Nuclear Magnetic Resonance)** and **LC-MS-NMR (Liquid Chromatography-Mass Spectrometry-Nuclear Magnetic Resonance)**, have gained significant attention in pharmaceutical analysis due to their ability to combine the strengths of multiple analytical methods, enabling comprehensive characterization of complex samples. These coupled systems provide the advantages of both separation and structural elucidation, offering enhanced capabilities for the identification, quantification, and analysis of pharmaceuticals, including drug formulations, metabolites, impurities, and degradation products. Over the years, significant advancements have been made in improving the sensitivity, resolution, automation, and applicability of these techniques in the pharmaceutical industry.

1. Advancements in LC-NMR and LC-MS-NMR

1.1 Sensitivity and Resolution:

- **Cryogenic NMR Probes**: Increased signal-to-noise ratio for detecting low-concentration compounds and trace impurities.
- **High-Field NMR Instruments**: Enhanced resolution for complex pharmaceutical

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samples, enabling better separation of closely related components.

1.2 Miniaturization and Microfluidic Devices:

- **Microfluidic LC Systems**: Reduced sample size and faster chromatographic separation, ideal for high-throughput screening.
- **Miniaturized NMR Systems**: Small sample requirements for high-throughput drug screening.

1.3 Integration with Mass Spectrometry:

- **LC-MS Coupling**: Provides molecular weight and structural information to complement NMR data.
- **LC-MS-MS**: Tandem mass spectrometry offers detailed structural data, especially for complex molecules[13].

2. Applications in Pharmaceutical Analysis

2.1 Drug Discovery and Development:

- **Metabolite Identification**: Helps identify metabolites and track drug metabolism in biological matrices.
- **Pharmacokinetics and ADME**: Crucial for understanding drug absorption, distribution, metabolism, and excretion.

2.2 Quality Control and Impurity Profiling:

- **Purity Analysis**: Identifies impurities and degradation products to ensure drug safety and efficacy.
- **Impurity Quantification**: Provides comprehensive analysis of drug formulations, improving quality control.

2.3 Stability Testing:

- **Degradation Studies**: Monitors drug degradation and stability under various conditions for shelf-life determination.
- **Forced Degradation**: Analyzes drug stability under stress to prevent future efficacy and safety issues.

2.4 Formulation Development:

- **Drug-Excipient Interactions**: Studies interactions to optimize bioavailability, stability, and solubility.
- **Polymorph Characterization**: Identifies and characterizes polymorphs, crucial for solubility and bioavailability.

3. Challenges and Future Directions

1. **Sensitivity and Data Interpretation**: Trace compound detection and the integration of complex chromatographic, NMR, and MS data require advanced software tools.
2. **Cost and Instrumentation**: High operational and maintenance costs remain barriers to widespread use.
3. **Automation and High-Throughput**: Further development of automation will improve efficiency and throughput in drug development and quality control[14].

II. CONCLUSION

In conclusion, advanced modern techniques in NMR spectroscopy, such as LC-NMR, LC-MS-NMR, DOSY-NMR, and qNMR, significantly enhance pharmaceutical analysis by offering high sensitivity, resolution, and non-destructive analysis capabilities. These innovations allow for more precise identification, quantification, and characterization of active pharmaceutical ingredients (APIs), excipients, metabolites, and impurities. They are critical for various stages of drug development, from discovery and formulation to quality control and stability testing. Advancements such as cryogenic probes, high-field instruments, microfluidic systems, and the integration with mass spectrometry have made these techniques more efficient and versatile. Automation and high-throughput capabilities further enhance their utility, enabling rapid and detailed analyses in pharmaceutical research and manufacturing. Despite some challenges, including sensitivity in complex mixtures and high operational costs, these cutting-edge NMR techniques are poised to play an increasingly central role in the pharmaceutical industry. As technology continues to evolve, NMR will remain a powerful tool for improving drug safety, efficacy, and quality.

REFERENCES

[1]. Yulia B. Monakhova, Ulrike Holzgrabe, Bernd W.K. Diehl, Current role and future perspectives of multivariate (chemometric) methods in NMR spectroscopic analysis of pharmaceutical products, Elsevier (2018) ;147: 580-589.

[2]. Janet Caceres-Cortes, Bradley Falk, Luciano Mueller,T G Murali Dhar, Perspectives on Nuclear Magnetic Resonance Spectroscopy in Drug Discovery Research, Journal of Medicinal Chemistry (2024) ; 67 (3) : 1701-1733.

[3]. B. Diehl, Principle in NMR Spectroscopy, Elsevier (2008) ; 1: 3-41.
[4]. Yun Peng, Zeting Zhang, Lichun He, Conggang Li & Maili Liu, NMR spectroscopy for metabolomics in the living system: recent progress and future challenges, springer nature link (2024) ; 416 : 2319-2334.
[5]. Da-Wei Li, Alexandar L. Hansen, Chunhua Yuan, Lei Bruschweiler-Li & Rafael Brüschweiler, DEEP picker is a deep neural network for accurate deconvolution of complex two-dimensional NMR spectra, Nature communications (2021).
[6]. Benjamin D. Harding, Alexander M. Barclay , Dennis W. Piehl , Ashley Hiett , Owen A. Warmuth , Ruixian Han , Katherine Henzler-Wildman ,Chad M. Rienstra, Cross polarization stability in multidimensional NMR spectroscopy of biological solids, Elsevier (2024) ; 365 : 107724.
[7]. Enping Lin, Zhemin Bai , Yifei Yuan, Zhiwei Chen , Yu Yang, Yuqing Huang, Zhong Chen, A General Reconstruction Method for Multidimensional Sparse Sampling Nuclear Magnetic Resonance Spectroscopy, The Journal of Physical Chemistry Letters (2021) ; 12(43) : 10622–10630.
[8]. Mingyue Li , Wei Xu , Yongchao Su, Solid-state NMR spectroscopy in pharmaceutical sciences, Elsevier (2021) ; 135 : 116152.
[9]. Rongchun Zhang, Wei Chen, Toshikazu Miyoshi, Elucidations of Structure and Molecular Dynamics of Complex Polymers by State-of-the-Art Solid-State NMR Spectroscopy, Macromolecules American Chemical Society (2024); 57 (5) : 1893-1918.
[10]. Yakugaku Zasshi , The Applications of qNMR in Drug Quality Control, Journal of the Pharmaceutical Society of Japan (2024) ; 144(4) :381-385.
[11]. Deyu Li , Ivan Keresztes , Russell Hopson , Paul G. Williard, Characterization of Reactive Intermediates by Multinuclear Diffusion-Ordered NMR Spectroscopy (DOSY), Accounts of Chemical Research (2009) ; 42(2): 270-280.
[12]. S V Kharlamov and Shamil K Latypov, Modern diffusion-ordered NMR spectroscopy in chemistry of supramolecular systems: the scope and limitations, Russian Chemical Reviews (2010) ;79 (8).
[13]. Chinaza Godswill Awuchi , Hannington Twinomuhwezi , Chibueze Gospel Awuchi , Hyphenated techniques, Academic press (2022) ; 125-145.
[14]. R Abhishek, SN Meyyanathan , Mohamed Musharaf B, Naveen RS, Sowbarnika S , Development of Natural Product by Different Hyphenated Techniques, High Technology Letters (2025) ; 31(1) : 1006-6748.