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Harnessing Mass Spectrometry for Molecular Analysis in Energy: From Fossil Fuels to Renewables

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Abstract

Mass spectrometry (MS) has become an indispensable tool for the detailed chemical analysis of materials used in energy production, spanning both traditional fossil fuels and modern renewable alternatives. This review explores advanced ionization sources and ultrahigh-resolution MS technologies in analyzing energy materials such as petroleum, biomass, biofuels, and bio-oil. Highlighted ionization techniques include electrospray ionization, atmospheric pressure chemical ionization, atmospheric pressure photoionization, laser desorption/ionization, and matrix-assisted laser desorption/ionization, all crucial for qualitative and quantitative assessments, as well as ultrahigh-resolution Fourier transform ion cyclotron resonance and Orbitrap mass analyzers. This review underscores the remarkable compositional detail achievable with state-of-the-art MS systems, providing molecular-level insights vital for advancing energy sectors. Introducing the concept of harvesting MS, we illustrate how these techniques can overcome challenges and optimize energy operations. Through case studies, this article highlights how these insights enhance energy production efficiency and sustainability, paving the way for future innovations.

1. INTRODUCTION

The pursuit of energy has driven significant technological advancements and economic growth, yet conventional sources like petroleum, coal, and natural gas pose substantial environmental and human health risks. In contrast, renewable energy sources such as biomass and biofuels offer a more sustainable alternative. As the world shifts toward cleaner energy due to the decreasing costs of renewable technologies and supportive policies, the need for precise and comprehensive analytical techniques becomes increasingly critical. Mass spectrometry (MS) has emerged as a pivotal tool in this context, enabling detailed chemical characterization of energy materials.

MS has played a significant role in energy analysis, especially in characterizing petroleum. The challenges faced by MS in unraveling the composition of these highly complex mixtures have driven significant advancements in methods and technologies. These advancements include innovative ionization sources, analyzers, and various MS techniques allowing precise molecular-level analysis. Among advancements in mass analyzers, ultrahigh-resolution mass spectrometry (UHRMS) stands out for its ability to provide detailed chemical characterization, enabling researchers to assign chemical compositions to numerous ions using direct infusion methods or hyphenated analytical techniques (1, 2).

Recent advancements have revolutionized compositional analysis with the development of Fourier transform mass spectrometry (FT-MS), leveraging improvements in superconducting magnet technology (3). FT-MS instruments deliver ultrahigh resolution, exceptional mass accuracy, and sub-parts-per-billion sensitivity, making them highly effective for analyzing complex mixtures from energy sources (4). Despite the successes of UHRMS techniques, including FT-MS instruments [Fourier transform ion cyclotron resonance (FT-ICR) and Orbitrap MS], challenges persist, particularly in sample preparation, ionization methods, structural identification, chromatographic separation, and data interpretation, which continue to be areas of intensive research.

UHRMS generates extensive datasets from complex mixtures, requiring advanced data processing techniques for thorough analysis. Chemometric methods and sophisticated software tools are essential for managing these vast data, with techniques such as Kendrick mass defect categorizing components based on heteroatom classes and double bond equivalents (DBEs). Software platforms aid in elemental composition assignments and enhance visualization through Van Krevelen and Kendrick plots. Innovative data pipelines for liquid chromatography (LC)-UHRMS-based petroleomics refine data interpretation, improving detection accuracy and reliability across various fuel types (5–9).

This review examines the exciting advancements and real-world applications of MS in analyzing various energy sources, including fossil fuels and renewables. We explore different ionization techniques such as electrospray ionization (ESI), atmospheric pressure chemical ionization (APCI), atmospheric pressure photoionization (APPI), laser desorption/ionization (LDI), and matrix-assisted laser desorption/ionization (MALDI), highlighting the game-changing impact of UHRMS using Fourier transform (FT-ICR and Orbitrap MS).

Our discussion delves into cutting-edge data analysis methods such as machine learning and statistical tools. Through case studies and practical examples, we show how molecular-level insights from these advanced spectrometric techniques can significantly optimize energy and fuel operations. We introduce the innovative concept of harvesting MS, showcasing how these techniques can be harnessed to address current challenges and limitations and pave the way for future breakthroughs in the field.

2. MASS SPECTROMETRY

2.1. Ionization Sources

The development of ionization sources operating directly at atmospheric pressure (API) has significantly expanded the scope and analytical applicability of MS. Among these sources, ESI, APCI, and APPI are widely used in energy resource analysis. Each technique captures a unique aspect of the chemical landscape, providing a comprehensive view of the sample's composition (7).

ESI applies a high voltage to a liquid sample, creating charged droplets that evaporate to produce ions, making it an ideal method for analyzing polar compounds such as proteins and small biomolecules (10). APCI involves spraying a solution through a heated capillary, where the analyte is vaporized and ionized by a corona discharge needle, making it suitable for low-to-medium-polarity analytes, including saturated hydrocarbons (11). APPI uses a vacuum ultraviolet lamp to ionize analytes by photoionization or charge transfer reactions (12), effective for nonpolar compounds and often used in analyzing fossil fuels and biofuels.

Together, these ionization techniques offer a complementary suite for analyzing diverse classes of compounds with distinct polarity and molecular mass ranges. While ESI covers a broad spectrum of polar compounds, APCI and APPI are tailored to less-polar analytes, each targeting specific molecular mass and polarity ranges. Specifically, APCI and APPI demonstrate effectiveness for low- to medium-polarity species, enhancing their applicability for certain fossil fuel components and renewable biofuels (13–15).

Laser-based ionization methods, such as MALDI and LDI, further expand MS capabilities in both traditional petroleum research and the innovative renewable energy sector. MALDI, which ionizes analytes embedded in a matrix through laser desorption, is well-suited for high-mass compounds, including proteins and synthetic polymers (16). LDI, which omits the matrix, instead directly irradiates the sample to ionize smaller molecules that absorb the laser energy, thus offering a rapid, matrix-free analysis pathway for low-molecular-weight compounds (17). Whereas MALDI excels in nonvolatile, high-mass compounds, LDI is optimized for smaller molecules that directly absorb laser energy, albeit within a more limited mass range.

Figure 1 illustrates this concept with a comparative diagram of the ionization sources, highlighting the molecular mass and polarity range covered by each ionization technique. This visual aid demonstrates how these techniques complement each other, each contributing to a complete picture of the chemical composition.

2.2. Ultrahigh-Resolution Mass Spectrometry

The analysis of complex mixtures, such as fossil fuels and renewable energy sources, demands UHRMS due to the intricate nature of their compositions. For example, FT-MS-based technologies such as FT-ICR and Orbitrap mass spectrometers offer unparalleled resolving power and mass accuracy that are essential for identifying and characterizing thousands of molecular components in these mixtures (18).

FT-ICR and Orbitrap instruments represent significant advancements over lower-resolution systems, with FT-ICR achieving up to 24 million in resolving power (19) and Orbitrap reaching 1 million (20). These instruments provide mass accuracy with errors as low as 0.5 ppm, a remarkable improvement over conventional systems such as quadrupole time-of-flight (Q-TOF), which typically offer resolutions below 100,000 and mass accuracies around 1 ppm. Such capabilities enable UHRMS systems to identify tens of thousands of unique species with heightened precision and sensitivity, a key advantage in analyzing complex matrices.

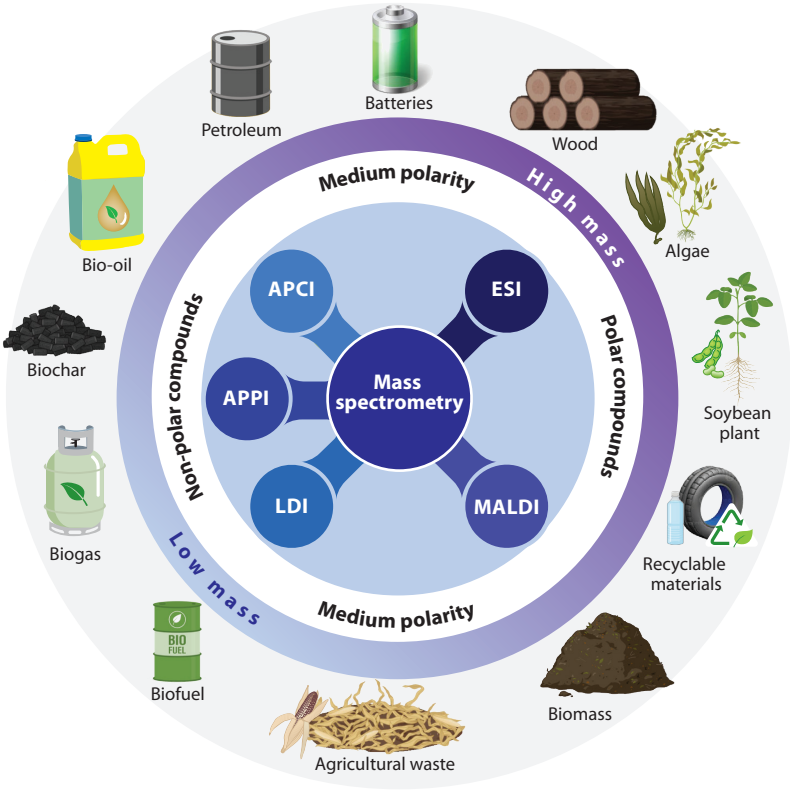


Figure 1

Comparative diagram of API sources, highlighting the molecular mass (*purple ring*) and polarity range covered by each API technique (*white ring*). The illustrations in the outer ring represent the different energy matrices in which mass spectrometry can be applied. Abbreviations: APCI, atmospheric pressure chemical ionization; API, atmospheric pressure ionization; APPI, atmospheric pressure photoionization; ESI, electrospray ionization; LDI, laser desorption/ionization; MALDI, matrix-assisted laser desorption/ionization. Figure adapted from image created in BioRender; Gontijo, B. 2025. **https://BioRender.com/l52i633**.

Figure 2 compares the number of publications in the last 10 years between FT-ICR and Orbitrap MS for fossil and renewable energy sources and their products, such as crude oil, gas oil, bitumen, diesel, jet fuel, coal tar, asphaltene, bio-oil, biodiesel, and biomass.

FT-ICR is widely used in petroleum studies and the analysis of various energy-related matrices, offering unparalleled insights into complex mixtures. Although Orbitrap also demonstrates versatility across numerous applications, FT-ICR remains the preferred technique for most energy sources, apart from biogas and jet fuel, where Orbitrap sees more frequent use (**Figure 2**). The high-resolution capabilities of both instruments are essential for understanding the chemical compositions and behaviors of these sources, supporting the development of more efficient and sustainable energy solutions.

These data (**Figure 2**) underscore the importance of selecting the appropriate MS technique based on sample complexity to achieve optimal analytical results. Although Orbitrap MS is effective for less-complex samples, offering a simpler and quicker analysis, FT-ICR MS excels with more complex samples such as crude oil, asphaltene, and vacuum residue due to its superior resolving power and mass accuracy. Thus, the choice between Orbitrap and FT-ICR MS should be

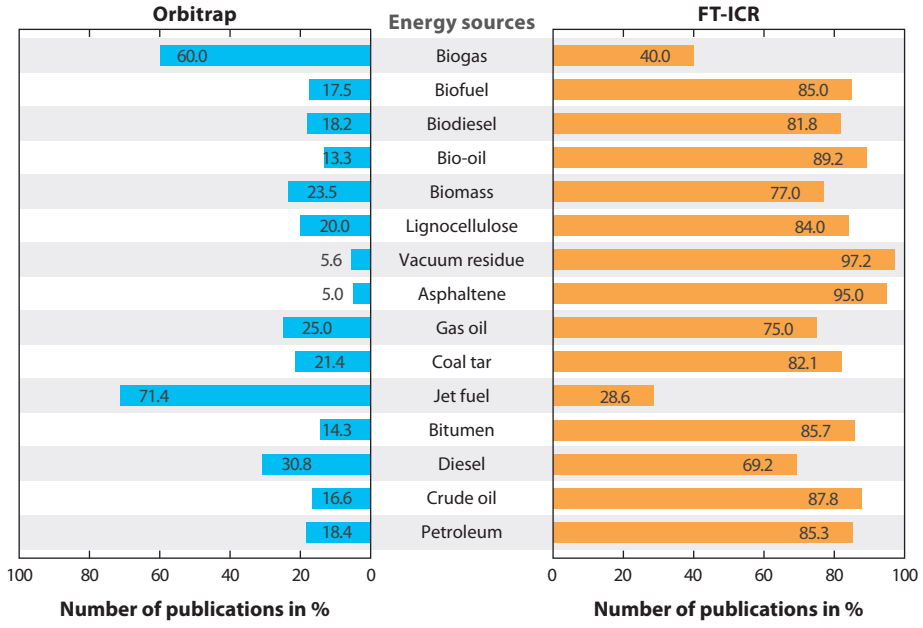


Figure 2

Journal articles published in the past 10 years (2014–2024) focusing on the application of Fourier transform ion cyclotron resonance (FT-ICR) mass spectrometry and Orbitrap mass spectrometry for the characterization of fossil and alternative fuels.

guided by the specific requirements of the sample matrix, balancing the need for detailed molecular information against the practical considerations of analysis time and resource availability.

2.3. Fourier Transform Ion Cyclotron Resonance

FT-ICR MS detects ions by measuring the image current produced as trapped ions rotate in a magnetic field at their cyclotron frequencies, providing unmatched resolving power and mass accuracy. Advances in FT-ICR MS are primarily due to superconducting magnet technology improvements and ICR cell design. Initially, FT-ICR used 2-T electromagnets, but modern instruments now employ magnets up to 21 T, significantly enhancing performance.

Although the 2-T FT-ICR instrument provided innovative, high-resolution capabilities for its time, it did not achieve the ultrahigh resolution possible today with higher magnetic field strengths and improved cell designs. The development of the dynamically harmonized FT-ICR cell has enabled resolving powers exceeding 10 million at a mass-to-charge ratio (m/z) of 1,000 with moderate magnetic fields around 7 T. Recently, efforts to further enhance resolving power have included increasing magnetic fields and employing multielectrode detection; however, a rise to 21 T did not yield a proportional improvement in resolving power (21). Future developments in hardware could push the resolution of top FT-ICR spectrometers to 100 million at m/z 1,000, driven by more vital magnetic fields and better ICR cell designs (22). Currently, FT-ICR systems are available with various magnetic fields, such as 7-T, 9-T, 15-T, and 21-T.

FT-ICR MS has been essential in analyzing complex mixtures of environmental organic molecules, including natural organic matter (23). Since its introduction by Comisarow & Marshall in 1974 (24), FT-ICR MS has been extensively used to study environmental organic matter at the molecular level. Its exceptional mass resolution and accuracy are critical for

distinguishing isobaric compounds, such as differentiating C_3 and SH_4, ^{13}CH and N, and O and CH_4. The high resolving power required for these distinctions and precise mass measurement makes FT-ICR MS indispensable for identifying unknown compounds within environmental organic matter. It remains the only MS technique capable of providing sub-parts-per-million mass accuracy for numerous peaks in complex mixtures (4).

Quadrupole (2ω) detection enhances the resolving power of FT-ICR mass spectrometers without increasing the magnetic field strength. Unlike the traditional detection setup, which uses two electrodes, 2ω detection involves four electrodes for signal acquisition. This configuration effectively doubles the resolution for the same acquisition time. For instance, Cho and colleagues (25, 26) achieved a resolving power of >1,000,000 at m/z 400 on a 7-T FT-ICR with 2ω detection. While this improvement is substantial, it does not fully replace the gains achieved with higher magnetic fields.

A comparative study analyzed residue oil samples using a 2ω 7-T FT-ICR and a 15-T FT-ICR instrument. The 2ω 7-T FT-ICR instrument demonstrated comparable performance in profiling complex samples, with superior signal intensities and reproducibility in absorption-mode processing. In the 7-T spectrum with 2ω detection, 16,247 peaks were identified, compared to 12,395 peaks in the 15-T spectrum. Conversely, the 15-T FT-ICR instrument provided more accurate elemental composition measurements (27).

The exceptional sensitivity, dynamic range, accuracy, resolution, and speed of FT-ICR are crucial for investigating the complex chemistry and dynamics of natural systems. The advancement to a 21-T FT-ICR instrument, for example, has led to exceptional mass accuracy and resolution, allowing for detailed characterization of natural organic matter. High-field FT-ICR MS such as 15-T and 21-T achieves the highest mass resolving power and accuracy available, with performance parameters such as resolving power and spectral acquisition rate improving linearly and mass accuracy and dynamic range improving quadratically with increased magnetic field strength. Thus, at high magnetic fields, spectral acquisitions can achieve resolving power exceeding 1 million and mass accuracy better than 1 ppm (18, 28).

A powerful example demonstrating the use of FT-ICR in petroleum sample analysis was provided in a study by Smith et al. (29), in which the investigators applied a 21-T FT-ICR mass spectrometer to analyze petroleum and dissolved organic matter. They demonstrated ultrahigh mass-resolving power ($m/\Delta m_{50\%}$ > 2,700,000 at m/z 400) with broadband root mean square (RMS) mass measurement accuracy less than 80 ppb, enabling the resolution and confident identification of tens of thousands of unique species. When the performance was compared to their custom-built 9.4-T FT-ICR instrument, the 21-T provided twofold-higher resolving power and sixfold-better mass accuracy, and it identified three times more molecular formulas in petroleum and dissolved organic matter analyses.

In the same study (29), the researchers demonstrated that the 21-T FT-ICR instrument detected 49,040 molecular formulas, compared to 29,012 at 9.4 T, including previously unresolved classes. Similarly, the analysis of dissolved organic matter benefited from the enhanced resolving power, which allowed for the distinction between doubly charged oxygen species and singly charged sulfur-containing species, requiring a resolving power exceeding 1,400,000 at m/z 600. This comparison underscores the ongoing demand for increased resolving power and improved mass accuracy to characterize the most complex organic mixtures comprehensively.

FT-ICR MS technology has revolutionized the molecular-level characterization of complex mixtures, such as heavy petroleum residues. Advances in this technique, as highlighted by Hsu et al. (30), have enabled UHRMS to achieve unprecedented accuracy in determining elemental compositions, significantly enhancing the ability to resolve and identify molecular species in intricate

systems. This technology is critical for understanding the chemical complexity of petroleum fractions and optimizing refining processes by identifying key molecular features and compositional differences across samples (30).

Figure 3 illustrates the power of FT-ICR MS through a detailed analysis of petroleum samples. **Figure 3*a*** illustrates broadband and mass-scale-expanded mass spectra of a characteristic petroleum sample analyzed using negative-ion ESI FT-ICR MS. The spectra reveal a wide distribution of molecular species across the *m/z* range of 150–800, highlighting the intricate chemical diversity of the sample. This high-resolution analysis identifies nitrogen-containing compounds (NCCs) and oxygen-containing compounds (OCCs) within a single spectrum, along with compounds containing multiple heteroatoms (31).

Figure 3*b* compares Chinese and South American crude oils at nominal mass 478 Da, highlighting distinct molecular profiles. Differences in the abundance and distribution of heteroatom-containing classes, such as nitrogen, oxygen, and sulfur species (e.g., NS and NO_2), are evident. The annotations of specific elemental compositions and expanded insets demonstrate FT-ICR MS's precision in resolving overlapping peaks.

Figure 3*c* emphasizes the quantitative advantages of the 21-T FT-ICR MS instrument over the 9.4-T system across various petroleum-related samples. **Figure 3*c*, subpanel *i*** shows the significant increase in molecular formula assignments with the 21-T instrument, particularly for samples with high heteroatom content. **Figure 3*c*, subpanel *ii*** details the enhanced identification of heteroatom-rich classes, such as N_1O_3, N_1O_4, and S_1O_3, enabled by the higher resolving power of the 21-T system. Finally, **Figure 3*c*, subpanel *iii*** illustrates the improved RMS mass assignment errors achieved with the 21-T system, ensuring more accurate molecular formula assignments (29).

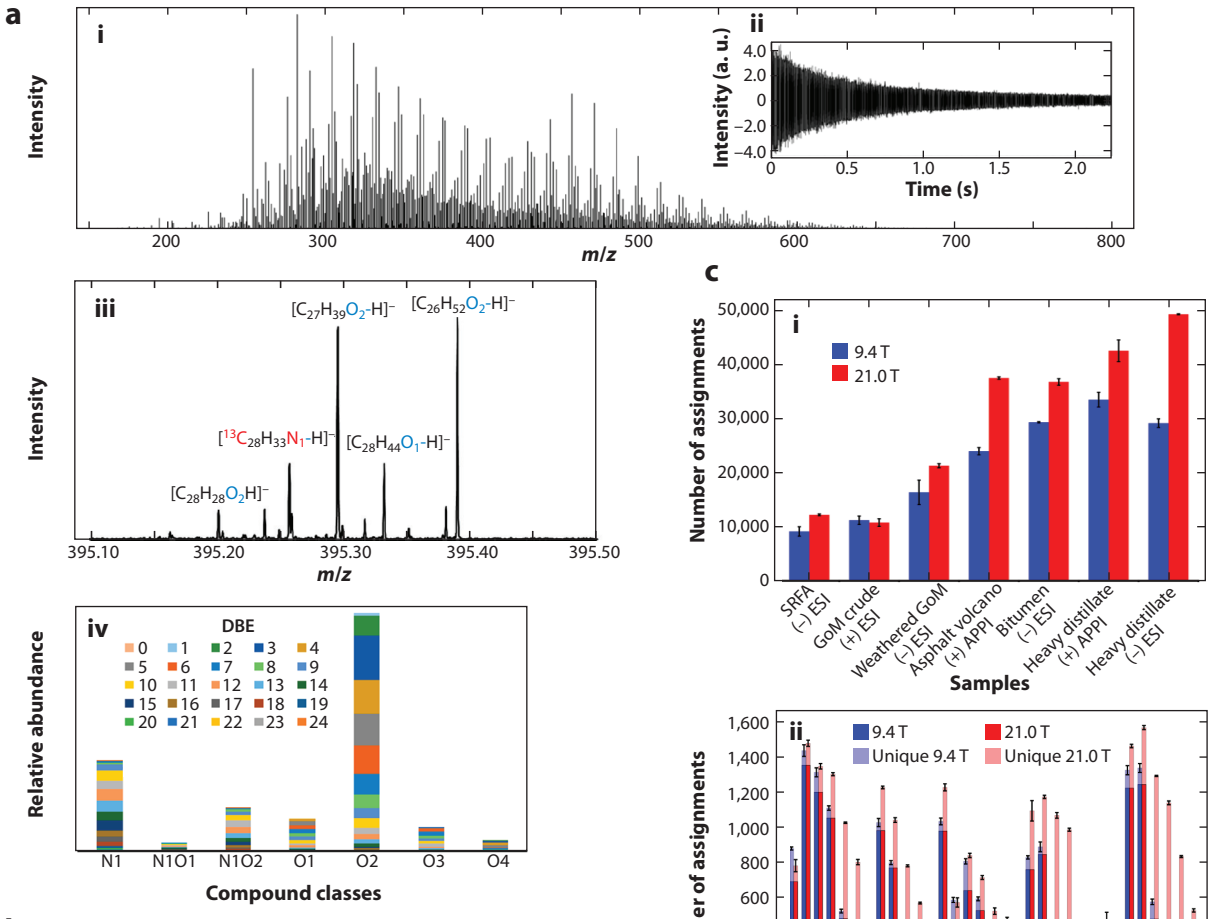
Together, the data presented in **Figure 3** demonstrate the versatility and analytical depth of FT-ICR MS in characterizing complex hydrocarbon mixtures. By integrating detailed spectral insights with comparative analyses, this technique provides a comprehensive understanding of crude oil composition and its implications for refining and product development. The ability to resolve molecular features with such high precision is invaluable for identifying compositional markers and optimizing processes to enhance the quality and efficiency of petroleum-derived products.

2.4. Orbitrap Mass Spectrometry

Orbitrap MS is another highly effective technology for analyzing complex mixtures due to its ultrahigh resolving power and precise measurement of *m/z* for numerous compounds. The Orbitrap mass analyzer works by trapping ions in an electrostatic field and measuring their oscillation frequency. The frequency is proportional to the ion's *m/z*, enabling high-resolution mass analysis. In this technique, ions are injected into a central electrode and then oscillate around it in a fixed frequency. The detector measures these oscillations, providing precise data on the ions' mass and abundance (32).

Orbitrap mass spectrometers are valued for their high resolving power, sensitivity, robustness, dynamic range, ease of calibration, and tandem mass capabilities. They offer high mass accuracy, up to 5 ppm with external calibration and 3 ppm with internal standards, simplifying pretreatment strategies for fast identification and quantitation in complex matrices (33). Its high mass resolution and accuracy facilitate the separation of isobaric compounds in complex mixtures and the assignment of their molecular composition.

Orbitrap MS provides powerful analytical capabilities by extending the detection range to include nonvolatile, thermally unstable, and highly polar acids and bases that are often challenging for gas chromatography (GC)-based methods (34). The Orbitrap mass analyzer is designed for precise ion control and image current detection. Since its introduction in the late 1990s,



(*Caption appears on following page*)

Figure 3 (*Figure appears on preceding page*)

(*a*) Overview of FT-ICR MS data and spectrum visualization. (*i*) Broadband mass spectrum, (*ii*) zoomed-in segment of the mass spectrum highlighting the ultrahigh resolution and precise identification of heteroatomic species, (*iii*) the FID signal used to generate the mass spectrum, and (*iv*) distribution of compound classes based on relative abundance, illustrating the chemical composition differences among the analyzed samples. Panel *a* adapted with permission from Reference 31; copyright 2021 American Chemical Society. (*b*) Zoomed-in mass insets of ultrahigh-resolution FT-ICR mass spectra of Chinese and South American crude oils at nominal mass 478 Da. This study focuses on the detailed molecular composition of heavy petroleum fractions, analyzing complex samples to identify specific chemical species. By comparing crude oils from different geographical origins, the research aims to reveal significant compositional variations that may affect their properties and refining behavior. Panel *b* adapted with permission from Reference 30; copyright 2011 John Wiley & Sons. (*c*) Quantitative comparison of 9.4-T and 21-T FT-ICR MS performance across diverse petroleum-related samples. (*i*) Total number of assigned molecular formulas, showing that 21-T FT-ICR MS allows for a greater number of molecular identifications. (*ii*) Detailed breakdown of heteroatom classes, with 21-T FT-ICR MS achieving more unique assignments. (*iii*) Comparison of RMS mass assignment errors, emphasizing the superior mass accuracy of the 21-T FT-ICR MS. These results highlight the crucial role of ultrahigh-resolution MS in the detailed molecular characterization of heavy petroleum fractions. Panel *c* adapted with permission from Reference 29; copyright 2018 American Chemical Society. Abbreviations: APPI, atmospheric pressure photoionization; DBE, double bond equivalent; ESI, electrospray ionization; FID, free induction decay; FT-ICR MS, Fourier transform ion cyclotron resonance mass spectrometry; GoM, Gulf of Mexico; RMS, root mean square; S/N, signal-to-noise ratio; SRFA, Suwannee River fulvic acid.

numerous high-performance MS instruments based on Orbitrap technology have emerged, categorized into single-stage, hybrid, and tribrid categories. Single-stage mass spectrometers, such as the Exactive Plus Orbitrap, provide a resolution of up to 140,000 FWHM. On the other hand, hybrid instruments, such as the Q Exactive series, integrate a quadrupole analyzer with an Orbitrap to enhance selectivity and overall performance.

This technology has been extensively applied in analyzing fossil and renewable energy sources. Despite its high resolution, the Orbitrap mass spectrometer offers lower resolving power compared to FT-ICR instruments, which limits its ability to detect a broad range of species in highly complex samples. This often necessitates the use of preseparation techniques to reduce sample complexity and enhance detection sensitivity (35). As such, many studies consider Orbitrap MS a complementary tool to FT-ICR MS for analyzing energy-related samples.

A recent study by Li et al. (36) proposed strategies for achieving quantitative analysis of compounds in heavy petroleum fractions, successfully assigning and quantifying more than 7,000 molecules across 20 different class species. This technology provides high resolution and resolving power and has been effectively applied to the in-depth analysis of complex mixtures, such as heavy petroleum fractions. It offers valuable insights into the structural details of hydrocarbons and heteroatomic compounds, which are essential for further processing.

3. APPLICATIONS IN FOSSIL FUELS

3.1. Petroleum and Crude Oil Analysis

Advances in MS, particularly in ionization methods and UHRMS technologies, have significantly enhanced the analysis and characterization of petroleum, enabling greater molecular coverage and more detailed chemical composition analysis. These technological advancements have provided new knowledge on the molecular composition of petroleum and oil samples that has helped elucidate geological processes that alter oil composition and have significant implications for the production sector.

New instrumental approaches using FT-ICR MS are expanding our understanding of petroleum geochemistry by enabling analysis of nonhydrocarbon species in crude oils. Oldenburg et al. (37) studied the impact of thermal maturity on nine crude oils, finding decreased NSO classes and increased aromaticity with thermal maturity. In the study, the investigators used a 12-T FT-ICR mass spectrometer with ESI and APPI sources to analyze crude oil, revealing

systematic changes in compound classes and potential molecular markers sensitive to maturity levels, including high molecular weight diamondoids. In another study (27), the authors investigated biodegradation processes in petroleum reservoirs, revealing both the breakdown and formation of compounds alongside variations in levels of hydrocarbons, sulfur- and nitrogen-containing compounds (SCCs and NCCs, respectively). Additionally, nitrogen isotope data suggested that nitrogen compounds in crude oil could act as nutrients for microorganisms, impacting the properties of the oil as biodegradation progresses (38).

Important petroleomics approaches for elucidating geochemical processes have been conducted by investigators at the German Research Centre for Geosciences (GFZ; Potsdam). A recent publication aimed to clarify the origin, thermal maturity, and alteration history of crude oils in the northern Western Desert of Egypt. Using a multianalytical approach, the research team identified five distinct oil families and differentiated oils based on their terrigenous, marine, or mixed organic matter origins. For example, OCCs were found to reflect the kerogen type and depositional conditions of the source rocks, with implications for understanding petroleum systems and biodegradation processes. These findings underscore the FT-ICR application in enhancing geochemical insights into complex crude oil compositions (39).

NCCs and OCCs serve as key indicators in geochemical evaluations. Deng et al. (40) demonstrated that ESI FT-ICR MS profiling of lacustrine oils effectively reflects crude oil maturity levels. Similarly, research by Covas et al. (41) and Oldenburg et al. (37) showed that polar compounds can be used to assess thermal maturity through ESI FT-ICR MS analysis. Additionally, FT-ICR MS has been widely employed in characterizing polar compounds in crude oils, providing insights into geochemical origins (42), organic matter biomarkers (43), and biodegradation stages (44).

MS, particularly ESI-MS in direct infusion mode, has been widely applied to study crude oil, offering powerful capabilities for characterizing and quantifying polar compounds across petroleum cuts and derivatives. For instance, ESI (–) FT-ICR MS has been employed to analyze polar compounds in crude oils from Brazilian pre- and post-salt reservoirs, revealing that the N_2, NO, and O compound classes are less abundant in post-salt oils, whereas the NO_2 and O_2 classes are slightly more prominent (45).

França et al. (46) also reported similar findings, showing high NCC content in pre-salt crude oils using ESI (±) Orbitrap MS. Both studies highlight FT-ICR MS as an effective method for differentiating crude oils from various geological sources, with implications for resource development and economic valuation. Likewise, Vaz et al. (44) demonstrated a method for classifying biodegradation levels in crude oils by analyzing O_2-containing compounds with ESI (–) FT-ICR MS, further underscoring the value of these advanced analytical techniques in petroleomics.

Although the NCCs and OCCs have been the most-studied components by ESI-MS, analysis of SCCs by ESI-MS has been reported over two decades. SCCs are less accessible by ESI-MS; however, the ionization of these compounds can be enhanced by online chemical derivatization or metal complexation (47). Maleki et al. (47) showed a method using silver attachment to sulfur atoms for ionization enhancement of SCCs combined with ion mobility–mass spectrometry (IM-MS) and FT-ICR MS to characterize SCCs in crude oil. The use of silver attachment in MS selectively ionizes SCCs, enhancing their mobility and producing less structural diversity compared to acid treatment, which favors ionization of amine-containing compounds; this selective affinity for sulfur helps in the accurate representation of sulfur-based ions in samples.

Application of MALDI in petroleum analysis has been significantly advanced by the development of simplified experimental procedures for isolating high-mass alkanes in crude oils. A method developed by Lorente et al. (48) involved forming urea-alkane adducts on chromatographic paper or silica plates, removing unreacted hydrocarbons and breaking the adducts with water. The isolated alkanes were analyzed by MALDI MS, showing improved detection sensitivity and range.

This technique effectively detected *n*-alkanes up to *m/z* 1,500 (C_{100}) with minimal use of sample and reagents such as $AgNO_3$ and urea.

Yuan et al. (49) utilized ESI FT-ICR MS to analyze shale oil, specifically focusing on ranking oil contributions from individual layers in a lacustrine shale oil system. Traditional geochemical methods do not provide sufficient performance to differentiate similar layers in a lacustrine shale oil system, but FT-ICR MS has proven effective for identifying thousands of nonhydrocarbon compounds. This method provides new geochemical fingerprints useful for tracking petroleum production in unconventional shale oil wells; however, its practical application remains limited. By comparing compositional similarities between rock extracts and produced oil and using multidimensional scaling, Yuan et al. successfully ranked the producing layers of a shale oil well in the Ordos Basin, China. This method shows promise for optimizing production strategies in shale oil systems (49).

Orbitrap MS provides detailed molecular characterization of heavy petroleum fractions but faces challenges in quantitative analysis due to inconsistent ionization efficiencies and mass discrimination during ion transmission. These issues arise from the dependence of ionization efficiency on structural diversity and the *m/z*, leading to discrepancies between ionized compounds and their actual concentrations. A recent study by Li et al. (36) addresses challenges in quantitative analysis of heavy petroleum fractions by proposing strategies that combine high-resolution Orbitrap MS with various ionization techniques, including positive- and negative-ion ESI, atmospheric photoionization, and chemical derivatizations for more accurate quantification of heavy petroleum fractions by normalizing molecular composition based on elemental data. The study focused on analyzing fluid catalytic cracking slurry decant oil and its fractions, employing an Orbitrap Fusion mass spectrometer equipped with various ionization techniques including ESI, APPI, and chemical derivatizations. The research successfully assigned and quantified more than 7,000 molecules across 20 different class species (36), including aromatic hydrocarbon and non-basic NO_3 class species.

3.2. Diesel and Jet Fuel

UHRMS techniques have been widely used for the detailed molecular characterization of diesel and jet fuel. One study (50) used FT-ICR MS to investigate polar organic compounds derived from diesel truck emissions, focusing on water-soluble organic compounds and dichloromethane-soluble organic compounds. These compounds were categorized into OCCs, NCCs, and SCCs based on their elemental compositions. The results of the study provided crucial insights into the molecular structures and compositions of water-soluble organic compounds and dichloromethane-soluble organic compounds, contributing valuable data for assessing the environmental impact of diesel truck usage (50). Understanding these emissions at a molecular level is key to developing strategies to mitigate their environmental impact.

Similarly, FT-ICR MS-based petroleomics approaches have been used to analyze diesel, kerosene, and residue fractions resulting from hydrothermal liquefaction (HTL) bio-crude integration into refinery operations with fossil crude. HTL bio-crude, derived from various biomass sources, offers high heating value and low heteroatom content but requires partial hydrotreatment to address high acidity and inorganic constituents. When blended with low-sulfur fossil oil at a 1:4 ratio, codistillation tests with pure fossil oil assessed the biomass feedstock's impact. Detailed molecular characterization demonstrated HTL bio-crude's significant influence on diesel, kerosene, and residue fractions (51). This study underscores the potential of integrating bio-crude into traditional refinery processes, which could help reduce the reliance on fossil fuels.

A study by Liu et al. (52) described a two-step degradation method to convert Powder River Basin coal into fuels, analyzing their chemical compositions using ESI FT-ICR. UHRMS data

revealed that O_1–O_4 class species dominate the light oil fraction. The study also highlighted the production of valuable carboxylic acids with total yields of 19.7 wt% through oxidation of the $scCO_2$/ethanol degradation residue in the second step. This approach offers an efficient pathway for coal conversion, aiming to produce fuels and chemicals while reducing energy consumption and environmental impact. This method demonstrates how UHRMS can be applied to improve the sustainability and efficiency of fuel production from unconventional sources.

Kong et al. (53) utilized FT-ICR MS to investigate the production of jet fuel precursors from waste kraft lignin via a depolymerization and hydrodeoxygenation process. The study employed a Bruker solariX XR with a 15-T magnet actively shielded superconducting magnet and a Bruker APEX with a 12-T actively shielded superconducting magnet to compare elemental distributions between kraft lignin and the optimized products. FT-ICR MS analysis focused on distinct species composed of carbon, hydrogen, and oxygen, assessing structural changes and product quality. The data obtained with advanced FT-ICR MS instrumentation highlights the detailed molecular transformations in converting biomass waste into valuable fuel precursors, showcasing the potential of sustainable aviation fuel production.

In addition, Commodo et al. (54) used ESI (+) FT-ICR MS to investigate the thermal oxidative stability of commercial aviation fuel, detecting various polar species in unstressed fuel and a large molecular mass band in stressed fuel. This study emphasizes the importance of oxidative stability in maintaining fuel quality and performance in aviation applications. An APCI-Orbitrap Fusion MS was used to analyze diesel, crude oil, and thiophene components in fuel. APCI enabled the analysis of thiophenes without derivatization, successfully ionizing these compounds in light fraction fuel and crude oil (55). These findings highlight the complementary role of Orbitrap MS to FT-ICR in analyzing SCCs, which is crucial for refining processes and improving fuel quality. Polar compounds of unprocessed and processed diesel samples were also investigated by Hughey et al. (56) using an ESI (+) FT-ICR MS instrument, resulting in the identification of approximately 500 elemental compositions.

A recent study (57) focused on analyzing ionized OCCs from jet fuel, diesel, and marine gas oil using ESI (–) linear quadrupole ion trap (LQIT)/Orbitrap MS. The study successfully identified up to nine, twenty, and nine homolog ion series of OCCs in jet fuel, diesel, and marine gas oil extracts, respectively. HRMS data allowed for detailed characterization of OCCs from jet fuel, diesel, and marine gas oil extracts, including determining molecular weights, aromatic rings and double bond equivalent, and carbon numbers for each OCC class (57). Advanced MS techniques including ESI LQIT/Orbitrap enabled identification and structural analysis of polar compounds in fuels, enhancing understanding of fuel chemistry and addressing issues related to storage, stability, and compatibility for improved performance and reliability.

3.3. Asphaltene, Bitumen, and Vacuum Residue Characterization

Asphaltene, bitumen, and vacuum residue are important heavy fractions obtained from crude oil, each with distinct chemical compositions and characteristics. Understanding the molecular structures of these materials is essential for optimizing their use in various applications, such as energy production and material development. These energy sources have been successfully characterized primarily using API FT-ICR MS. Extensive research has been conducted to elucidate the chemical composition of these materials, and numerous studies have demonstrated the applicability of ESI in the characterization of crude samples and their fractions (58–60).

In recent years, significant interest has been shown in asphaltene analysis, another heavy fraction obtained from crude oil, particularly in the context of developing novel asphaltene-based materials across various domains (61–63). Generally, asphaltenes are insoluble parts separated by adding *n*-alkane solvents and demonstrate complex chemical composition and structures (63).

Therefore, understanding the molecular structures of asphaltenes, which cause pipeline blockages and catalyst fouling, is crucial. However, their relative abundances are debated, often due to the limitations of MS studies that generalize findings based on a narrow range of ionized asphaltenes (64).

A study performed by Dong et al. (64) used medium-energy collision-activated dissociation in an Orbitrap mass spectrometer to analyze asphaltene ions across different *m/z* values in asphaltene samples and few model compounds. The results showed varying abundances of single- and multicore compounds, indicating that traditional MS may suffer from sampling bias. In contrast, in-source collision-activated dissociation avoids this bias by not requiring ion selection.

Klein et al. (65) reported the application of ESI (±) FT-ICR MS to differentiate asphaltenes collected from two geographic locations (a North American land-based well and a Permian Basin) based on their polar composition. Pereira et al. (66) analyzed Brazilian asphaltene samples using different ionization techniques. The authors have shown that each technique provides access to a unique chemical profile of compound classes. Recently, Nyadong & Mendez-Arroyo (67) highlighted the ESI (+) MS technique for screening porphyrins directly from asphaltenes by using sodium formate as an ESI dopant modifier.

When analyzing asphaltene using ESI, a problem arises due to the solvent compatibility between those required for stable ESI sprayed solution, which involves polar solvents (e.g., methanol), and those that solubilize asphaltenes, generally nonpolar solvents such as benzene and toluene. Altering the solvent systems to facilitate ESI destabilizes asphaltene solutions, leading to precipitation in the ESI capillary (66).

The structural analysis of vacuum residues from different geological sources (Taching, Sumatra light, Iranian heavy, Arabian mix, and Murban) was carried out using ESI FT-ICR MS without chromatographic preseparation. This method identified basic nitrogen and nitrogen–sulfur compounds, revealing differences in molecular weights and hydrogen deficiency indices, which varied by origin. Notably, Taching residues exhibited a lower hydrogen deficiency index compared to other Middle Eastern samples (68). In a separate study, a Venezuela Orinoco vacuum residue was fractionated into 13 subfractions, and comprehensive chemical composition was analyzed by ESI FT-ICR MS. The analysis showed that as the subfractions increased in molecular weight, they also showed higher aromaticity and were enriched in multifunctional groups such as N_1S_1, N_1S_2, and N_1O_1. These findings demonstrate the distinct molecular characteristics of vacuum residues, with heavier fractions containing larger asphaltene molecules, as confirmed by additional saturate, aromatic, resin, and asphaltene (SARA) fractionation and gel permeation chromatography analyses (69).

MALDI-TOF analysis was used to study the molecular weight distribution (MWD) changes in vacuum residue, bitumen, and pyrolyzed fuel oil during visbreaking (70). This technique allows rapid sample preparation and analysis for solid and liquid analytes. The study highlighted shifts in MWD sections indicating cracking reactions predominating over condensation and polymerization. Vacuum residue displayed a peak around 400 *m/z*, while bitumen and pyrolyzed fuel oil showed narrower MWD ranges, indicating lighter compositions. MALDI-TOF analysis proved effective in characterizing MWD variations, suggesting its promise for heavy oil research in both laboratory and industrial settings (70).

4. APPLICATIONS IN RENEWABLE ENERGY SOURCES

4.1. Biomass and Biofuel Analysis

Biomass analysis has traditionally been challenging for conventional technologies because its matrix is highly complex and not well-characterized, necessitating more advanced and comprehensive

methods for accurate characterization and understanding. Reymond et al. (71) tackled the inherent complexities of biomass analysis by designing an online LC × LC system coupled with IM-MS to enhance carbohydrate separation from lignocellulosic biomass. This setup allowed for a more detailed characterization of sample components beyond the capabilities of conventional methods. The study marked a pioneering effort by implementing reverse-phase liquid chromatography (RPLC) × RPLC-IMS-HRMS hyphenation, which overcame the challenges associated with handling four-dimensional data. This approach significantly enhanced compound separation, especially for coeluting species, and provided specific descriptors (two retention times, mobility descriptor, and mass spectrum) to support confident identification of analytes, thereby advancing the level of analytical precision and confidence in biomass characterization (71).

Organic matter from lower aquatic organisms can be converted into biomass energy. Han et al. (72) explored the geochemical characteristics of Mesoproterozoic source rocks in North China, aiming to advance the understanding of organic matter composition and maturity in these ancient formations. Using FT-ICR MS, the study identified a high abundance of type I–III organic matter, which is indicative of a predominantly immature to low-maturity stage, with the potential for generating aromatic crude oil. The authors leveraged hydrocarbon biomarkers and polar compounds to assess the maturity and hydrocarbon-generation potential. Results showed that the chemical composition of organic compounds was significantly influenced by depositional conditions and maturity levels. As maturity increased, FT-ICR MS revealed a notable rise in DBE and carbon numbers in detected compounds, along with variations in specific structures such as carbazoles, benzofurans, and thiophenes, providing valuable insights into the potential of these rocks as hydrocarbon sources in Mesoproterozoic systems (72).

FT-ICR MS was used to examine and classify bio-oil molecules in different lignocellulosic-based biomass pyrolysis processes, providing a detailed molecular profile. Complementing this, high-performance thin layer chromatography (HPTLC) analyzed bio-oils' molecular composition, highlighting their typically high oxygen content. Advanced pyrolysis methods, such as fast pyrolysis, catalytic fast pyrolysis, and reactive catalytic fast pyrolysis (RCFP), are essential to improve bio-oil quality by reducing oxygen content. This study investigated these methods using a combination of FT-ICR MS and HPTLC, which allowed for a comprehensive analysis of bio-oil derived from each pyrolysis type, offering insights into how different pyrolysis processes affect bio-oil composition and quality (73).

LDI FT-ICR MS was applied directly on solid samples of biomass and biochar derived from lignocellulosic sources such as Douglas fir and *Miscanthus*, allowing for in situ analysis without the need for sample preparation. This technique, with a spatial resolution of approximately 100 μm, enabled an examination of the effects of laser conditions (specifically, wavelength and irradiance) on the mass spectra obtained. At lower laser irradiance, the analysis primarily highlighted subunits of biomass, such as cellulose and lignin derivatives. In contrast, higher irradiance revealed a broader range of compounds, including thermal pyrolysis products and species resulting from gas-phase recombination, such as polycyclic aromatic hydrocarbons and other complex aromatic structures. These findings offer a deeper understanding of the molecular composition of biomass and the various chemical transformations occurring during pyrolysis (74).

4.2. Bio-Oil Characterization

Bio-oils derived from plants are a promising renewable energy source owing to their ability to produce biofuels and other valuable chemicals. As such, characterizing their constituents is of high importance. Negative-ion mode ESI is particularly effective for analyzing bio-oils, as their polar compounds can be readily deprotonated to form $[M\text{-}H]^-$ ions (75, 76). Most of the applications of

the ESI-MS technique in the characterization of bio-oils include determining their chemical composition from different feedstocks or processes, bio-oil aging, and selectivity of biofuel upgrading using various methodologies (75, 77–80).

Tessarolo et al. (81) reported the applicability of the ESI (−) FT-ICR MS to study the chemical composition of bio-oils from two natural sources: empty palm fruit and pine wood chips. The study identified different $C_xH_yO_z$ compound classes in both samples. Oxygen atoms count distributions were similar, with O_5 species prominent and related to sugar derivatives in both samples. On the other hand, O_2 compounds were observed only in the empty palm fruit bio-oil and corresponded to fatty acid molecules. NCCs detected in the palm fruit bio-oil were likely sugar-derived components coupled with nitrogen-containing secondary pyrolysis products. Phenolic compounds were present in both samples. In another study, Santos et al. (82) conducted bio-oilomics analyses to elucidate the polar composition of second-generation liquid biofuels obtained from the micropyrolysis process of freshwater plants by ESI (±) FT-ICR MS. The N_2 and O_2 classes obtained via ESI (+) and the O_2 and O_3 classes obtained via ESI (−) were the significant classes detected in the samples.

Recently, Mase et al. (73) applied ESI FT-ICR MS to analyze three bio-oils produced by different pyrolysis processes of pinewood residue pellets: fast pyrolysis, catalytic fast pyrolysis, and RCFP. The authors summarized that the RCFP process was the best process for producing oils with a low O/C ratio. Chacón-Patiño et al. (78) also demonstrated the petroleomics-based approach in the field of renewable energy by employing ESI (±) FT-ICR MS in the molecular characterization of nonvolatile species from a loblolly pine bio-oil and its hydrotreated effluents.

Inclusion of bio-oils in conventional refineries is an attractive approach to increase the green carbon content in traditional fossil fuels and products, supporting efforts toward more sustainable energy sources (77, 83, 84). However, relatively few studies have explored the specific outcomes of coprocessing bio-oils with petroleum streams using ESI-MS (85). Pontes et al. (86) investigated the chemical speciation of blends containing vacuum residue and bio-oil using ESI (±) Orbitrap MS, demonstrating the potential of ESI for detecting renewable polar molecules incorporated into vacuum residue. Their results revealed that bio-oil addition led to a notable increase in polar compound classes, including oxygenated and nitrogenated species, enhancing the complexity of the vacuum residue matrix. This coprocessing approach highlighted the potential for integrating bio-oil components into petroleum streams, showing that renewable molecules could be successfully embedded in vacuum residue, thereby promoting sustainable modifications in refining processes.

An FT-ICR MS-based petroleomics approach was employed to analyze the molecular composition of upgraded products derived from pyrolysis bio-oils using high-field FT-ICR MS equipped with a 12-T superconducting magnet and a dynamically harmonized ICR cell (78). The study focused on nonvolatile compounds from loblolly pine bio-oil and its hydrotreated derivatives, leveraging soft ionization methods. ESI allowed the evaluation of polar oxygen-containing molecules. At the same time, APCI enabled the study of hydrocarbons. Significant temporal changes in specific molecular species, such as alkylated and oxygenated aromatic compounds, were observed during hydrotreatment. The study demonstrated that high-activity hydrodeoxygenation catalysts effectively transformed bio-crude into fuel-range products, suggesting that advanced petroleomics methods can be instrumental in optimizing renewable fuel production (78).

Nunes et al. (87) conducted a comprehensive chemical characterization study of bio-oils derived from the HTL of sugarcane bagasse using ESI (±) Orbitrap HRMS and hyphenated techniques. The HTL process was explored under various conditions, including different temperatures and residence times, with or without a catalyst, and recycling. The bio-oils, evaluated

using GC × GC-TOF MS and ESI (±) Orbitrap HRMS, exhibited diverse chemical composition comprising phenols, ketones, furans, aldehydes, carboxylic acids, and esters. These compounds significantly impact the bio-oil's combustion performance, storage stability, upgrading response, and economic value, underscoring the need for sensitive and selective analytical techniques to address its complex composition.

A recent study (88) demonstrated the effectiveness of MALDI and LDI techniques for analyzing bio-oils derived from lignocellulosic biomass. Using FT-ICR MS, it was shown that MALDI provided more comprehensive information than LDI, as evidenced by a greater number of attributed molecular formulas (e.g., 1.5–6 times more for oxygenated species when using dithranol, acetosyringone, or graphene oxide as matrices). The selectivity of various MALDI matrices was assessed, with dithranol, acetosyringone, and graphene oxide emerging as the most effective, offering detailed molecular characterization of bio-oils, including lignin derivatives, sugars, and lipid derivatives. This work highlighted MALDI's potential to provide a thorough molecular description of bio-oils.

4.3. Batteries

With rising environmental concerns and the demand for reliable portable power, sustainable energy and efficient energy storage technologies have become crucial. In this context, researchers focus on converting solar, mechanical, waste heat, and wind energy into electricity, with rechargeable Li-ion, Na-ion, and Mg-ion batteries playing a pivotal role. These batteries store energy through redox reactions, with energy density determined by electrode capacity and cell voltage. Although Li-ion batteries are famous for their high energy density and good cycling ability, enhancing their energy density further is essential. Addressing degradation issues in high-capacity cathodes and developing safer electrolytes are critical for advancing battery technology, especially for electric vehicles (89–91).

The high volume of published research on Li-ion batteries has facilitated advanced studies into the various species produced during cycling. A study performed by Gachot et al. (90) aimed to understand the aging processes of Li-ion batteries to enhance their lifespan and safety. ESI HRMS was used to identify organic species from the degradation of carbonate-based electrolytes at low potentials, revealing the formation mechanisms of ethylene oxide oligomers. GC-MS was also employed to investigate highly volatile compounds. The combined techniques enabled the researchers to propose a comprehensive electrolyte degradation scheme, highlighting the crucial role of HRMS in identifying degradation products and understanding their formation pathways.

Li-ion batteries are vital for electric vehicles, requiring enhancements in fast charging, energy density, safety, and longevity. Understanding degradation mechanisms is key to improving performance and lifespan. A recent study analyzed electrolytes from Li-ion battery cells by five global manufacturers using ion chromatography, GC, and MS techniques. This study aimed to optimize Li-ion battery reliability in electric vehicles by characterizing electrolyte composition and identifying degradation products under realistic conditions (92). Using LC-HRMS, the study investigated the complex decomposition of state-of-the-art Li-ion battery electrolytes and identified new routes involving reactive species (92).

GC-MS analysis of gas evolution in Li-ion batteries revealed that delithiated positive electrodes generated substantial CO_2, whereas in fully charged cells, the negative electrode effectively consumed CO_2. Notably, the study identified that CO_2 generated by the positive electrode might migrate to the negative electrode, where it reacts and reduces the total gas volume within the cell. This interaction was shown to play a crucial role in minimizing gas production and maintaining cell integrity under high temperatures and voltages (93).

MS and its hyphenated techniques allow detailed analysis of electrolyte composition, decomposition products, and battery interfacial processes. These techniques provide precise identification and quantification of chemical species, offering insights into chemical changes and degradation pathways, ultimately aiding in the development of more robust and efficient battery systems.

In summary, the comprehensive analysis of energy-related materials, including both fossil fuels and renewable energy sources, relies not only on advanced mass analyzers and ionization sources but also on robust separation techniques. Although mass analyzers and ionization sources are discussed in greater depth, separation techniques such as high-performance liquid chromatography (HPLC) and GC are also widely used in the energy sector. These methods, often coupled with MS, provide complementary information on the chemical composition of complex mixtures.

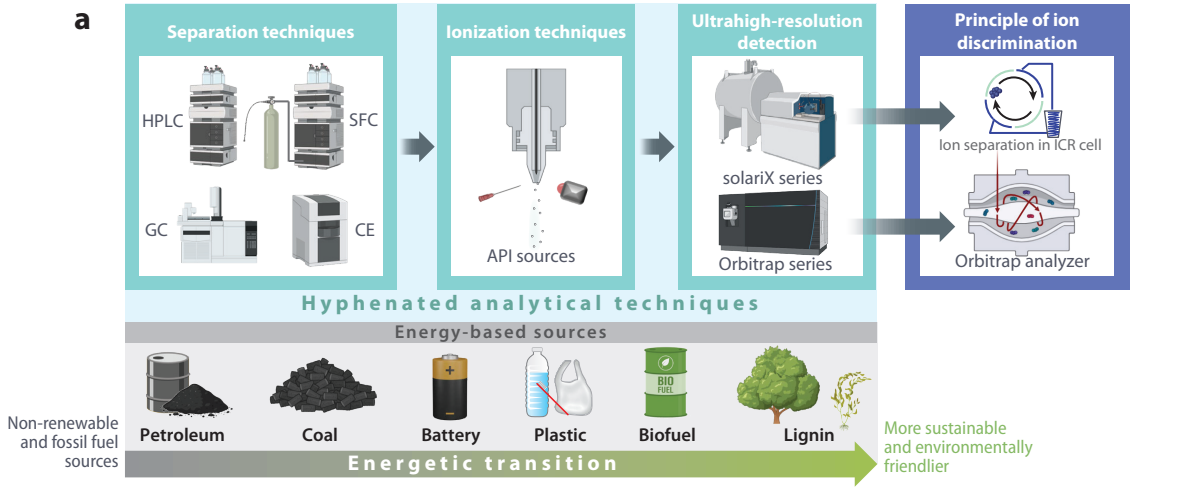
Hyphenated analytical techniques, which combine advanced separation methods with high-resolution detectors like FT-ICR MS and Orbitrap MS instruments, play a pivotal role in the precise isolation and detailed characterization of chemical compounds. The use of ionization sources such as ESI, APCI, and APPI is integral to this process, as they effectively ionize both polar and nonpolar molecules, thereby expanding the diversity of detectable chemical species.

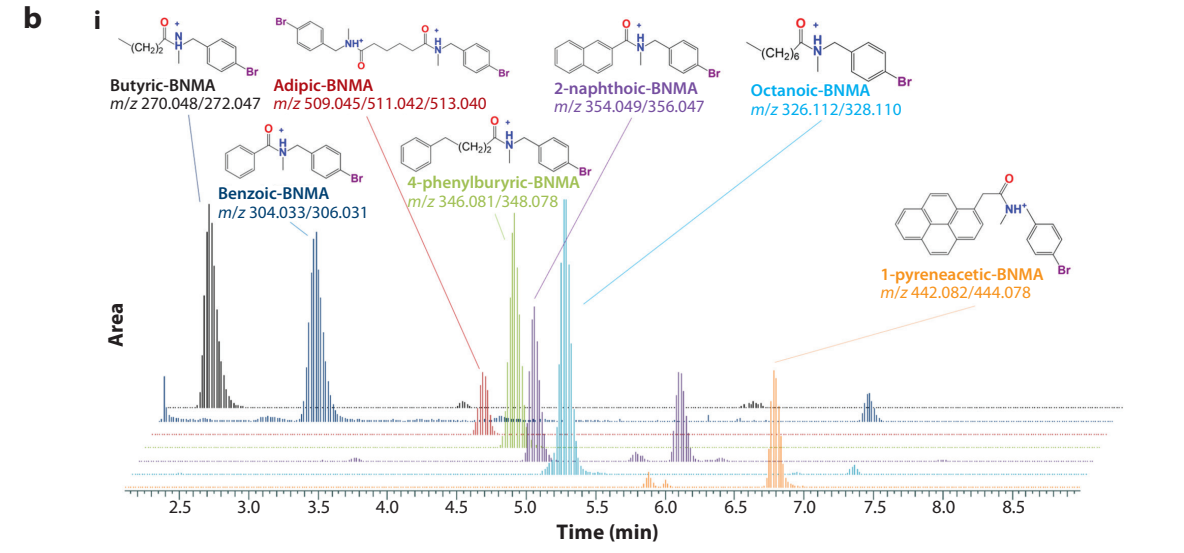
These techniques are particularly relevant in the context of the energy transition, as shown in **Figure 4**, which illustrates a spectrum of energy sources, ranging from conventional options such as petroleum and coal to emerging alternatives. Built upon this base, the figure outlines the critical components of the analytical workflow, including separation techniques [HPLC, GC, supercritical fluid chromatography (SFC), and capillary electrophoresis (CE)], ionization methods (ESI, APCI, and APPI), and high-resolution detectors (solariX and Orbitrap series).

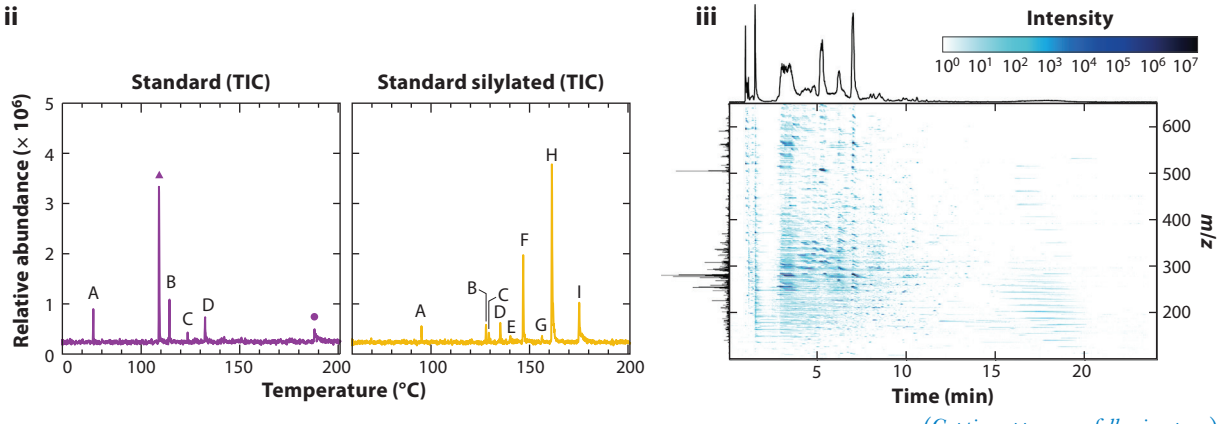
Recent studies emphasize the transformative potential of these methods to address challenges within the energy sector. Huynh et al. (94) developed a methodology for profiling carboxylic acids in crude oil using LC-ESI Orbitrap MS combined with selective derivatization by 4-bromo-*N*-methylbenzylamine (4-BNMA). As depicted in **Figure 4*b***, **subpanel *i***, the derivatization produces a distinctive ion pair (*m/z* 169/171), enabling the isolation and identification of carboxylic acids in complex mixtures. This approach simplified data processing and detected up to 380 carboxylic acids in six Danish North Sea crude oils, including fatty acids, aromatic acids, and polyfunctional acids, demonstrating the method's effectiveness for nontargeted screening of complex energy-related matrices.

In another study, Vesga Martínez et al. (95) explored the use of GC-Orbitrap MS with silylation to enhance the analysis of polar compounds in bio-oils (**Figure 4*b***, **subpanel *ii***). Silylation significantly improves the thermal stability and ionization efficiency of compounds, facilitating the differentiation of isotopologs through detailed isotopic fine structures. This advanced workflow also addresses challenges in resolving isobaric species, highlighting the utility of prolonged transient data acquisition in molecular characterization.

With a similar objective, Devaux et al. (3) applied SFC-FT-ICR MS to characterize bio-oils derived from microalgae (**Figure 4**, **subpanel *iii***). This method excels in separating isomeric species that are challenging to differentiate using direct introduction techniques. The incorporation of quadrupole detection further enhances resolution and acquisition rates, allowing for comprehensive molecular descriptions of bio-oils. The study demonstrates how hyphenated techniques can classify compounds based on retention times and heteroatom content, such as fatty acid derivatives and nitrogen-containing species, contributing to advancements in sustainable energy research (3). The last two studies underline the critical role of hyphenated analytical techniques in driving innovation and providing detailed molecular insights, thereby supporting the global transition to sustainable energy solutions.







(*Caption appears on following page*)

Figure 4 (*Figure appears on preceding page*)

(*a*) Schematic representation of the role of hyphenated analytical techniques in energy transition research and their applications in molecular characterization. (*Top*) Key components of hyphenated workflows, including separation techniques (HPLC, GC, SFC, and CE), ionization sources (ESI, APCI, and APPI), and UHRMS detectors (solariX and Orbitrap series). Panel adapted from image created in BioRender; Gontijo, B. 2025. **https://BioRender.com/l52i633**. (*b*) Specific applications are highlighted: (*i*) profiling carboxylic acids in crude oil through selective derivatization with 4-BNMA, enabling detailed molecular characterization using LC-ESI Orbitrap MS. Panel adapted with permission from Reference 94; copyright 2024 American Chemical Society. (*ii*) Impact of silylation on isotopic differentiation and detectability of polar compounds in bio-oils analyzed using GC-Orbitrap MS. The numbers in the non-silylated and silylated graphs correspond to a set of standard compounds detectable via resonance-enhanced multiphoton ionization at 248 nm. The compounds highlighted in purple include guaiacol (A), eugenol (B), p-anisic acid (C), and acetovanillone (D). The yellow-labeled compounds include guaiacol (A), eugenol (B), phenylacetic acid (C), p-anisic acid (D), isoeugenol (E), acetovanillone (F), syringaldehyde (G), vanillic acid (H), and syringic acid (I). The • symbol indicates an additional peak corresponding to a thermal degradation or rearrangement product with the molecular formula $C_{13}H_{16}O_4$. Panel adapted with permission from Reference 95; copyright 2024 American Chemical Society. (*iii*) Characterization of microalgae bio-oils using SFC-FT-ICR MS with quadrupole detection, demonstrating the separation of isomeric species and classification by heteroatom content. Panel adapted with permission from Reference 3; copyright 2024 American Chemical Society. Abbreviations: 4-BNMA, 4-bromo-*N*-methylbenzylamine; APCI, atmospheric pressure chemical ionization; API, atmospheric pressure; APPI, atmospheric pressure photoionization; CE, capillary electrophoresis; ESI, electrospray ionization; FT-ICR MS, Fourier transform ion cyclotron resonance MS; GC, gas chromatography; HPLC, high-performance liquid chromatography; ICR, ion cyclotron resonance; LC, liquid chromatography; MS, mass spectrometry; *m/z*, mass-to-charge ratio; SFC, supercritical fluid chromatography; TIC, total ion chromatogram; UHRMS, ultrahigh-resolution MS.

5. HARNESSING MOLECULAR INFORMATION TO ENERGY AND FUELS OPERATIONS

In petroleomics, use of the Kendrick mass defect has significantly advanced complex mixture analysis by categorizing components based on heteroatom classes, DBEs, carbon number versus DBE, alkylation levels, and drift time versus *m/z* (6, 96). In addition, modern software tools such as Python and R enable interactive data handling and visualization, supporting statistical methods such as principal component analysis and volcano plots for interpreting petroleomics data and identifying significant peaks (6, 96).

The vast amount of mass spectral data generated from complex energy source samples with UHRMS requires the use of sophisticated software, platforms, and chemometric methods for processing, elemental composition assignments, and handling data dimensionality beyond conventional software capabilities. Developing data analysis methods is challenging due to the variability in data and the critical choice of the ionization source, which determines the detectable compounds. To address these challenges, numerous software programs and advances in artificial intelligence have been developed.

A powerful tool for this application is the software PetroOrg, which was designed for processing and visualizing IM-MS data of crude oil. It excels in handling bidimensional IM-MS datasets and automating elemental composition assignments. PetroOrg facilitates the comparison of IM-MS datasets recorded with various API sources. The software enables detailed analysis by assigning elemental compositions to ultrahigh-resolution spectra and bidimensional IM-MS data. It can display data as different 2D plots, such as DBE or drift time versus carbon number. This capability is crucial for characterizing heavy petroleum samples, increasing overall peak capacity, and providing valuable information on isomeric content (7).

An alternative software essential for petroleomics data analysis is PyC2MC, an open-source resource developed for visualizing and processing UHRMS data of complex mixtures. Created by the international complex matrices molecular characterization joint lab (iC2MC), this modern software uses Python 3.9.7 and popular libraries such as pandas, NumPy, and SciPy. PyC2MC offers a user-friendly graphical interface via PyQt5 and can be used either as a prepacked executable or by running the Python script. Available on GitHub and Zenodo, it supports rapid data

plotting, Kendrick mass defect plot generation, and environmental variable representation. It is accessible to nonprogrammers and open for community improvements. Its effectiveness has been demonstrated on various sample types, making it a valuable tool for MS data analysis (97).

A novel data processing pipeline for LC-HRMS-based petroleomics data has been developed to address the limitations of existing tools. This pipeline includes a customizable formula database from detected samples, reducing redundancy and interference. Key features include the extraction of chromatographic information, removal of false-positive assignments using chromatographic information such as retention, and effective mining of low-abundance components. The method provides multidimensional information, such as heteroatom class, DBE, carbon number, retention time, and tandem MS spectra, significantly improving detection coverage and reliability (98). In summary, this pipeline offers a comprehensive and reliable solution for the molecular characterization of petroleum samples, enhancing the understanding of chemical variations in refining processes.

These platforms, software, and processing pipelines are essential tools for analyzing complex samples using HRMS data. They accelerate data processing while ensuring transparency and traceability, making them powerful resources for conducting reliable and efficient research in petroleomics. In this context, a web-based software named DropMS designed to streamline the processing and analysis of HRMS data for petroleomics was developed. It significantly reduces processing time and integrates essential algorithms for spectral preprocessing, noise removal, mass recalibration, chemical formula assignment, isotopic validation, and data visualization. The software processes mass spectra and visualizes data with popular diagrams such as Van Krevelen and Kendrick plots. DropMS facilitates data organization by importing directly from manufacturers, supports multisampling diagrams, and utilizes chemometrics for enhanced MS data analysis (8).

The primary challenge in analyzing complex mixture data lies in the large dataset size, often exceeding gigabytes, and the intricate composition of datasets, which reflects immense chemical diversity. To address these challenges, researchers use chemometric approaches, employing statistical methods and machine learning techniques in a data analysis pipeline to interpret mass spectra efficiently (99). Applications in energy sources include profiling chemicals, discriminating samples, determining fuel properties, and assessing geochemical processes (45, 100, 101). Recent advancements in technology have heightened interest in mathematical and machine learning models as potential solutions.

The use of artificial intelligence for data analysis is transforming the petroleum industry by enhancing exploration, development, production, and reservoir management, leading to faster decision making and cost reduction (102). Artificial intelligence, combined with HRMS data, plays a transformative role in the energy sector by enabling more precise geochemical analysis and enhancing data interpretation for crude oil characterization, supporting informed decision making, and optimizing hydrocarbon recovery (103). In this context, various methods combined with multivariate calibration have been applied to quantify crude oil properties. For instance, Vaz et al. (44) employed FT-ICR MS and chemometric analysis to classify crude oils based on their biodegradation levels, focusing on the O_2 class of naphthenic carboxylic acids, and introduced the acyclic to cyclic carboxylic acid index and saturated carboxylic acid index to effectively monitor biodegradation trends in oil mixtures.

A notable study (104) in this field used UHRMS data to distinguish the origins of crude oil, incorporating chemometric data treatments to extract geochemical insights. The analysis focused on crude oil maltene fractions using GC × GC-QMS (quadrupole MS) and employed statistical methods such as support vector machine discriminant analysis (SVM-DA), partial least squares discriminant analysis (PLS-DA), and others to classify oils according to their lacustrine or marine organic matter origins. The statistical analysis focused on the overall geochemical information

derived from the maltene fraction of crude oils, which include various isoprenoid derivatives and biomarkers. SVM-DA demonstrated superior performance in discriminating against crude oils. This approach offers a robust alternative to conventional techniques, emphasizing the role of chemometrics in petroleum fingerprinting and suggesting avenues for future improvements in analytical strategies (104).

6. FUTURE DIRECTIONS AND INNOVATIONS

Emerging technologies in MS are transforming the analysis of energy sources by offering comprehensive analytical capabilities. IM-MS stands out for its ability to perform rapid, multidimensional analysis, providing detailed structural information essential for precise molecular identification in complex samples such as petroleum (47). This technique complements traditional MS methods by resolving isomeric compounds and revealing supramolecular interactions that influence material properties (47, 105, 106).

Alongside IM-MS, advanced chromatographic techniques such as two-dimensional chromatography with selective stationary phases enhance separation efficiency and peak capacity, enabling deeper characterization of energy source compositions (71). Additionally, novel ionization technologies such as field ionization/field desorption and APCI are expanding mass spectrometric capabilities by effectively ionizing diverse compound classes such as saturates compounds and large nonvolatile polyaromatic molecules within complex mixtures (107). In addition, chemometric methods and advanced data analysis software further contribute by mining vast datasets from complex mixtures, extracting relevant information crucial for the energy sector. These advancements collectively enhance our ability to comprehensively analyze and understand the chemical makeup and origins of energy sources.

Despite advancements in petroleomics and complex mixture analysis, challenges persist. Different ionization methods provide insights into varied compound types, but desorbing intact molecules from solid samples such as asphaltene deposits remains problematic due to the molecular complexity and strong interactions within solid matrices such as asphaltene deposits, which can hinder the desorption and ionization of intact compounds. Quantification is hindered by factors such as ionization efficiencies, matrix interferences, and the diverse isomeric nature of components. As petroleum production shifts toward unconventional sources such as heavy oil, oil sands, and shale oil, analysis of these heavier and more complex samples demands higher resolving power and advanced fragmentation techniques. These methods are essential for accurately characterizing the diverse molecular compositions typical of such sources. Handling vast datasets from HRMS data, especially when coupled with chromatographic separation, continues to challenge data processing and visualization tools crucial for comprehensive analysis across diverse applications (96).

Future directions in MS for petroleum analysis emphasize optimizing ionization methods and refining fractionation techniques before analysis. Ongoing research aims to enhance these methods and mass spectrometric instrumentation, particularly using UHRMS spectrometers to differentiate elemental compositions in petroleum compounds from varied origins, thermal evolution, and formation mechanism. The integration of automated chemometrics, predictive analytics, and data visualization tools is crucial to effectively interpret the vast amount of chemical data generated. These advancements are poised to tackle current and future challenges in the petroleum industry, improving the accuracy and depth of petroleum sample analysis (2).

7. CONCLUSIONS

The increasing demand for renewable energy sources driven by incentivizing policies underscores the necessity for rapid analytical methods to ensure fuel composition. This review emphasizes the

versatility and critical role of MS in analyzing a broad spectrum of energy sources, including classical fossil fuels, pyrolytic bio-oils, and biodiesel. MS techniques encompassing various methods of sample introduction, ionization sources, and mass analyzers position it as a cornerstone in energy and fuels research. UHRMS facilitates the resolution of complex mixtures and precise chemical formula attribution, while chromatographic techniques and IM-MS offer unparalleled isomeric speciation and sample complexity reduction. The last two decades have seen significant advancements in mass spectrometric techniques, particularly in soft ionization methods that preserve analyte integrity. These developments have propelled the analysis of petroleum fractions, enabling detailed compositional insights and improved modeling of complex systems.

In summary, recent advancements in HRMS, coupled with chromatographic techniques and combined with chemometric approaches, have significantly improved the chemical characterization of energy sources such as petroleum. These innovations address challenges such as ion suppression, isomeric separation, and selective ionization, enhancing the precision and accuracy of analyses. Additionally, the development of advanced data analysis tools and artificial intelligence applications has revolutionized petroleomics, enabling detailed molecular-level insights. These technological improvements are essential for optimizing crude oil recovery, refining processes, and decision-making within the petroleum industry. Overall, MS continues to evolve, enhancing our understanding and quality control of diverse energy materials.

DISCLOSURE STATEMENT

The authors are not aware of any affiliations, memberships, funding, or financial holdings that might be perceived as affecting the objectivity of this review.

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