Egyptian Knowledge Bank
https://ijmti.journals.ekb.eg/

International Journal of Materials Technology and Innovation
Volume 4, Issue 1 (2024), pages 42-74

Online ISSN 2682-4299

Analytical Techniques for Determining Pesticide Residues in Food: A Comprehensive Review

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Received ……20 June 2024
Accepted ……25 June 2024
Published ..…29 June 2024

Abstract

Pesticides play a crucial role in modern agriculture by enhancing crop yield and protecting crops from pests. However, the indiscriminate use of pesticides has raised concerns about their potential adverse effects on human health and the environment, particularly through residues in food. Analytical methods are essential for monitoring pesticide residues in food to ensure compliance with safety regulations and to protect consumers. This review provides an overview of analytical techniques employed to determine pesticide residues in food, focusing on advances in instrumentation, sample preparation, and detection methods. Various chromatographic, spectroscopic, and mass spectrometric techniques are discussed, highlighting their strengths and limitations. Additionally, emerging technologies such as biosensors and nanomaterial-based approaches are explored for their potential applications in pesticide residue analysis. The review also addresses challenges and future perspectives in the field, emphasizing the need for continued research and innovation to improve detection sensitivity, selectivity, and efficiency in pesticide residue analysis.

Keywords: Pesticides, Food Safety, Analytical Techniques, Chromatography, Spectroscopy, Mass Spectrometry, Biosensors, Nanomaterials.

List of Abbreviations

(DART)	Direct Analysis in Real-Time	(MAE)	Microwave-Assisted Extraction
(DESI)	Desorption Electrospray Ionization	(MIPs)	Molecularly Imprinted Polymers
(DLLME)	Dispersive Liquid-Liquid Microextraction	(MRLs)	Maximum Residue Limits
(ECD)	Electron Capture Detector	(MS)	Mass Spectrometry
(ELISA)	Enzyme-Linked Immunosorbent Assay	(MS/MS)	Tandem Mass Spectrometry
(FID)	Flame Ionization Detector	(MSPD)	Matrix Solid-Phase Dispersion
(FTIR)	Fourier Transform Infrared Spectroscopy	(NIR)	Near-Infrared Spectroscopy
(GC)	Gas Chromatography	(NMR)	Nuclear Magnetic Resonance Spectroscopy
(GC-MS)	Gas Chromatography-Mass Spectrometry	(PLE)	Pressurized Liquid Extraction
(HRMS)	High-Resolution Mass Spectrometry	(RSD)	Relative Standard Deviation
(ICA)	Immunochromatographic Assays	(SBSE)	Stir Bar Sorptive Extraction
(ICP)	Inductively Coupled Plasma Spectroscopy	(SFE)	Supercritical Fluid Extraction
(LOD)	Limit Of Detection	(SPE)	Solid-Phase Extraction
(LOQ)	Limit Of Quantification	(SPME)	Solid-Phase Microextraction
QuEChERS	(Quick, Easy, Cheap, Effective, Rugged, And Safe)	(UV-Vis)	Ultraviolet-Visible Spectroscopy

IJMTI vol. 4, issue 1 (2024) 42-74 https://doi.org/10.21608/IJMTI.2024.298332.1105

1. Overview of Pesticide Residues in Food

Agricultural practices extensively utilize pesticides to protect crops from pests, diseases, and weeds. These chemicals are designed to eliminate target organisms but may also threaten human health and the environment. Residual traces of these pesticides can remain in or on food products post-treatment [1]. Pesticide residues are commonly detected in various food items, including fruits, vegetables, grains, meat, poultry, dairy products, fish, and seafood [2]. The accumulation of these residues in the human body over time is concerning due to potential adverse health effects [3]. Thus, it is crucial to monitor and analyze pesticide residues in food to ensure they remain within safe limits and pose no risk to consumers [4].

Pesticide residue analysis in food involves the detection, identification, and quantification of certain pesticides or their degradation products. This is done using various analytical techniques capable of separating, identifying, and quantifying individual pesticide compounds in complex food matrices [5, 6].

Analytical techniques for pesticide residue analysis can be broadly classified into four categories: chromatographic techniques, spectroscopic techniques, mass spectrometry techniques, and immunoassay techniques [7-9].

Gas chromatography (GC) and liquid chromatography (LC) are extensively employed in pesticide residue analysis[10,7,11]. These methods separate pesticide compounds based on their distinct physical and chemical properties, facilitating their identification and quantification. GC is ideal for analyzing volatile and semi-volatile pesticides, whereas LC is better suited for polar and non-volatile pesticides.

Ultraviolet-visible (UV-Vis) spectroscopy and infrared (IR) spectroscopy are spectroscopic techniques that rely on light interacting with pesticide molecules. These methods offer insights into the chemical structure and functional groups of pesticide compounds, aiding their identification.[12-13, 14-16].

Mass spectrometry (MS) techniques are known for their high sensitivity and selectivity in analyzing pesticide residues [17-21]. MS allows for the determination of molecular weight and fragmentation patterns of pesticide compounds, facilitating their identification and quantification. Commonly utilized techniques include gas chromatography-mass spectrometry (GC-MS) [19, 22] and liquid chromatography-mass spectrometry (LC-MS) [19, 23-25] for pesticide residue analysis.

Immunoassay techniques, such as enzyme-linked immunosorbent assay (ELISA) [26-28], rely on specific antibody binding to pesticide molecules. These methods are rapid and cost-effective but may not match the sensitivity and selectivity of chromatographic and mass spectrometry techniques. Immunoassays are typically employed as screening tools to detect pesticide residues in food samples swiftly.

In addition to analytical techniques, sample extraction, and cleanup procedures are crucial in pesticide residue analysis. These methods involve extracting pesticide residues from food matrices and eliminating interfering substances to enhance analysis accuracy and reliability [29-32]. Common extraction techniques include solvent extraction [33], solid-phase extraction (SPE) [23, 34-36], QuEChERS (Quick, Easy, Cheap, Effective, Rugged, and Safe) [37-42], matrix solid-phase dispersion (MSPD) [43, 44], and supercritical fluid extraction (SFE) [33, 45].

Once the pesticide residues have been extracted and cleaned up, they can be analyzed using the appropriate analytical technique. The choice of technique depends on factors such as the type of pesticide, the concentration range of interest, and the desired sensitivity and selectivity.

This review aims to provide insights into the analysis of pesticide residues in food which is essential for ensuring food safety and protecting human health. Analytical techniques play a crucial role in detecting and quantifying pesticide residues in various food products. These techniques, along with sample extraction and cleanup techniques, enable the accurate and reliable analysis of pesticide residues, helping to ensure that food products are within acceptable limits and safe for consumption.

Importance of Pesticide Residue Analysis

Pesticides play a vital role in agriculture by safeguarding crops against pests, diseases, and weeds, thereby ensuring food security and enhancing agricultural productivity. However, these chemicals also present potential risks to human health and the environment. Pesticide residues refer to the remnants of these chemicals that persist in or on food products following their application. Monitoring and analyzing pesticide residues in food are essential steps in ensuring food safety and protecting consumer health. These

measures are critical for maintaining consumer well-being and safeguarding the environment.

Ensuring Food Safety

The main objective of conducting pesticide residue analysis is to safeguard the safety of the food supply. Pesticides are formulated to be toxic to pests, and their residues can potentially harm humans if consumed in excessive quantities. The presence of pesticide residues in food can result in acute or chronic health consequences, such as nausea, vomiting, dizziness, and even cancer. Hence, it is essential to ascertain the levels of pesticide residues in food to ensure they comply with permissible limits established by regulatory bodies. This ensures that food remains safe for consumption and protects public health.

Compliance with Regulatory Standards

Regulatory agencies globally have set Maximum Residue Limits (MRLs) for pesticides in food products [2, 46]. These limits specify the maximum allowable concentration of pesticide residues that can legally remain in food. Pesticide residue analysis is crucial for ensuring adherence to these regulatory standards. By analyzing food samples for pesticide residues, food producers, processors, and regulatory authorities can verify whether residue levels comply with the established limits. If residues exceed the MRLs, appropriate measures can be implemented to mitigate risks and prevent the sale of contaminated food products [47]. This ensures that consumers are protected from potential health hazards associated with excessive pesticide residues in food.

Monitoring Environmental Impact

Pesticides can cause significant environmental harm, including soil, water, and air contamination [48]. Analyzing pesticide residues in food offers important insights into the environmental impact of pesticide use in agriculture [49, 50]. By monitoring residue levels in food, scientists and environmental agencies can evaluate the extent of pesticide contamination in the environment and initiate measures to address these issues. This may include implementing more stringent regulations, advocating for sustainable farming practices, or promoting organic farming methods [51-53]. These efforts are crucial for mitigating the environmental consequences associated with pesticide use and fostering sustainable agricultural practices.

2 Methods for Pesticide Residue Analysis

2.1 Sampling and Sample Preparation for Pesticide Residue Analysis

Sampling and sample preparation are crucial steps in pesticide residue analysis as they directly impact the accuracy and reliability of the results. These steps ensure that representative samples are obtained from the food matrix and that any interfering substances are removed or minimized before analysis [30].

Sampling

Sampling involves collecting representative samples from a larger population of food items to accurately reflect pesticide residue levels across the entire group. Proper sampling techniques are crucial for obtaining reliable results that can be generalized to the broader food supply [54].

When designing a sampling plan, several factors must be considered, such as the type of food, target analytes (pesticides), sampling location, and desired level of confidence in the results. It is essential to determine a statistically significant sample size that is representative and ensure samples are collected in a random and unbiased manner.

Sampling can occur at different stages of the food production chain, including farms, during transportation, at processing facilities, or at retail outlets. Selecting sampling locations should consider potential contamination sources and how pesticide residues are distributed within the food matrix [55]. This approach helps in effectively monitoring and managing pesticide residue levels throughout the food supply chain.

Once the samples have been collected, they need to be properly handled and stored to prevent degradation or contamination. This includes using appropriate containers, labeling them correctly, and storing them at the appropriate temperature to maintain sample integrity [44, 56, 57].

Sample Preparation

Sample preparation is the method of preparing a food sample to make it suitable for analysis. This process typically includes several steps, such as homogenization, extraction, and cleanup [30, 56].

Homogenization involves reducing the sample size and ensuring it accurately represents the entire food item [58]. This step is particularly critical for solid samples like fruits, vegetables, and grains.

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Homogenization can be achieved through mechanical methods such as grinding or blending or through enzymatic or chemical treatments to break down the sample matrix. By homogenizing the sample, its consistency and composition become uniform, enabling accurate and representative analysis of pesticide residues and other contaminants.

Extraction is the process of isolating the target analytes from the food matrix. Typically, this is achieved using a solvent or a blend of solvents capable of selectively dissolving pesticide residues. The selection of extraction solvent depends on the chemical characteristics of the analytes and the composition of the food matrix. Common solvents used include acetone, methanol, and acetonitrile [29, 33, 59].

Fig. 1 The steps involved in determining pesticides.

Cleanup represents the final stage of sample preparation and involves eliminating interfering substances that could affect the accuracy of the analysis. This step is crucial for complex food matrices containing high levels of fats, proteins, sugars, and other compounds that might interfere with the analysis. Cleanup techniques include solid-phase extraction, liquid-liquid extraction [60], and methods like QuEChERS (Quick, Easy, Cheap, Effective, Rugged, and Safe) [42, 61]. These techniques ensure that the extracted samples are purified and ready for precise pesticide residue analysis.

The choice of sample preparation technique depends on several factors, including the type of food matrix, the target analytes, and the desired level of sensitivity. It is important to select a method that can effectively extract the pesticide residues while minimizing the loss or degradation of the analytes.

2.2 Chromatographic Techniques for Pesticide Residue Analysis

Chromatographic techniques are essential in the analysis of pesticide residues in food due to their exceptional sensitivity, selectivity, and capability to separate complex mixtures of compounds [7]. These methods enable precise identification and quantification of pesticide residues, ensuring accurate assessment of food safety standards.

Gas chromatography (GC)

Gas chromatography (GC) is particularly well-suited for analyzing volatile and semi-volatile compounds. In GC, compounds are separated based on their volatility and interaction with a stationary phase. The process begins with the sample being vaporized and injected into a heated column, where the compounds separate according to their boiling points. Detection occurs using specialized detectors such as a flame ionization detector (FID) or an electron capture detector (ECD).

GC is commonly employed for analyzing pesticides like organochlorines, organophosphorus compounds, and pyrethroids. However, it is less suitable for polar compounds and compounds that are sensitive to high temperatures.

2.3 Spectroscopic Techniques for Pesticide Residue Analysis

Spectroscopic techniques are pivotal in the analysis of pesticide residues in food, leveraging the interaction between electromagnetic radiation and matter to yield insights into chemical composition and structure. These methods are prized for their sensitivity, selectivity, and capacity to analyze multiple compounds concurrently. In this context, we will delve into several widely employed spectroscopic techniques for pesticide residue analysis [12, 62].

2.3.1 UV-Visible Spectroscopy

UV-Visible spectroscopy is extensively employed for pesticide residue analysis, relying on the measurement of light absorption or transmission in the ultraviolet and visible regions of the electromagnetic spectrum. Pesticide residues absorb light at specific wavelengths, enabling their detection and quantification. This technique is valued for its simplicity, cost-effectiveness, and speed in delivering results. However, UV-Visible spectroscopy has limitations regarding sensitivity and selectivity, as it

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cannot distinguish between closely related compounds [63].

2.3.2 Fourier Transform Infrared Spectroscopy (FTIR)

Fourier Transform Infrared Spectroscopy (FTIR) is a robust technique used for analyzing pesticide residues. It operates by measuring the absorption of infrared radiation by pesticide residues, which reveals details about their functional groups and chemical structure. FTIR is effective in identifying and quantifying various pesticide residues present in food samples. It is non-destructive and demands minimal sample preparation.

FTIR is renowned for its high sensitivity, specificity, and capability to analyze intricate mixtures. However, interpreting FTIR data may require specialized training and expertise [64].

2.3.3 Raman Spectroscopy

Raman spectroscopy is a versatile technique employed for analyzing pesticide residues in food. It revolves around the scattering of laser light by pesticide molecules, generating a distinctive Raman spectrum used for identification and quantification purposes. This spectroscopic method offers valuable insights into the chemical composition and molecular structure of pesticide residues.

Raman spectroscopy stands out for being non-destructive and requiring minimal sample preparation. It is renowned for its high sensitivity, selectivity, and capability to analyze samples in situ. However, Raman spectroscopy may necessitate intricate data analysis and can be susceptible to fluorescence interference [65].

2.3.4 Nuclear Magnetic Resonance Spectroscopy (NMR)

Nuclear Magnetic Resonance Spectroscopy (NMR) is a potent technique for analyzing pesticide residues in food. It harnesses the magnetic properties of atomic nuclei to yield comprehensive insights into the chemical structure and composition of pesticide residues. NMR is effective in both identifying and quantifying pesticide residues within complex matrices.

This nondestructive spectroscopic method requires minimal sample preparation. NMR is esteemed for its high resolution, sensitivity, and capability to analyze mixtures. Nonetheless, its effective use may require specialized equipment and expertise for accurate data interpretation [64, 66-68].

2.3.5 Fluorescence Spectroscopy

Fluorescence spectroscopy is a highly sensitive and selective method for analyzing pesticide residues in food. This technique measures the emission of fluorescent light by pesticide molecules when excited with specific wavelengths of light. It can effectively identify and quantify pesticide residues even in complex matrices.

Fluorescence spectroscopy is nondestructive and typically requires minimal sample preparation. It is recognized for its exceptional sensitivity, selectivity, and capability to analyze samples in real time. However, fluorescence spectroscopy may encounter challenges such as background fluorescence interference, necessitating careful optimization of experimental conditions to ensure accurate results [69-72].

2.3.6 Near-Infrared Spectroscopy (NIR)

Near-infrared spectroscopy (NIR) is a rapid and non-destructive method used for analyzing pesticide residues in food. This technique measures the absorption and reflection of near-infrared light by pesticide residues, providing valuable information for identification and quantification. NIR spectroscopy is renowned for its speed, simplicity, and capability to analyze samples directly in situ. It is particularly advantageous for large-scale screening and quality control applications across various food samples. However, successful implementation of NIR spectroscopy may necessitate calibration models to ensure accurate results. Additionally, it can be influenced by sample heterogeneity, requiring careful consideration during analysis [73-76].

2.3.7 Inductively Coupled Plasma Spectroscopy (ICP)

Inductively Coupled Plasma Spectroscopy (ICP) is a robust technique employed in the analysis of pesticide residues in food. This method involves the atomization and ionization of pesticide residues within an argon plasma, followed by the measurement of their emission or absorption spectra.

ICP spectroscopy is highly effective for identifying and quantifying a broad spectrum of pesticide residues, including heavy metals. It is esteemed for its exceptional sensitivity, selectivity, and capacity to

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concurrently analyze multiple elements. However, ICP spectroscopy necessitates specialized equipment and expertise for both operation and data interpretation [77, 78]. This technique is particularly valuable in ensuring the safety and compliance of food products with stringent regulatory standards concerning pesticide residues and heavy metal contaminants.

In conclusion, spectroscopic techniques are valuable tools for the pesticide residues analysis in food. They provide rapid, sensitive, and selective analysis of pesticide residues, allowing for the identification and quantification of multiple compounds simultaneously. Each spectroscopic technique has its own advantages and limitations, and the choice of technique depends on the specific requirements of the analysis. Utilizing spectroscopic techniques is essential for researchers and analysts to guarantee food safety and quality by effectively monitoring and controlling pesticide residues.

2.4 Mass Spectrometry Techniques for Pesticide Residue Analysis

Mass spectrometry (MS) is a potent analytical technique extensively employed in pesticide residue analysis owing to its exceptional sensitivity, selectivity, and capability to offer structural insights into analytes. This versatile method can be coupled with various separation techniques like gas chromatography (GC) or liquid chromatography (LC) to enhance the analysis of intricate samples [17, 19].

2.4.1 Gas Chromatography-Mass Spectrometry (GC-MS)

Gas chromatography-mass spectrometry (GC-MS) is a widely used technique for pesticide residue analysis. In GC-MS, the sample undergoes initial separation by gas chromatography based on the analytes' volatility and polarity. Subsequently, the separated compounds are introduced into the mass spectrometer, where they undergo ionization and fragmentation. The resulting ions are then detected and analyzed to identify and quantify the target analytes [22, 79]. GC-MS offers several advantages in pesticide residue analysis. It achieves excellent separation of analytes, making it suitable for analyzing complex samples with significant matrix interference. The mass spectrometer provides high sensitivity, enabling the detection of trace levels of pesticides in food samples. Furthermore, the mass spectra obtained from GC-MS are valuable for identifying and confirming analytes based on their unique fragmentation patterns [80]. This combination of separation power and sensitive detection makes GC-MS a cornerstone technique in pesticide residue analysis, ensuring reliable and accurate results.

2.4.2 Liquid Chromatography-Mass Spectrometry (LC-MS)

Liquid chromatography-mass spectrometry (LC-MS) is a widely utilized technique for pesticide residue analysis. In LC-MS, the sample undergoes initial separation by liquid chromatography based on the polarity and hydrophobicity of the analytes. Subsequently, the separated compounds are introduced into the mass spectrometer, where they undergo ionization and detection [19, 21, 81].

LC-MS offers numerous advantages in pesticide residue analysis. It accommodates a broad spectrum of analytes, including both polar and nonpolar compounds, which makes it well-suited for analyzing diverse pesticide residues in food samples. LC-MS also provides exceptional sensitivity and selectivity, facilitating the detection and quantification of trace levels of pesticides in complex matrices. The mass spectra obtained from LC-MS are instrumental for identifying and confirming analytes based on their distinct mass-to-charge ratios and fragmentation patterns [82, 83].

Overall, LC-MS is a powerful and versatile technique that enhances the capability to analyze pesticide residues comprehensively and accurately, ensuring food safety and regulatory compliance.

2.4.3 Tandem Mass Spectrometry (MS/MS)

Tandem mass spectrometry (MS/MS) is a potent technique that combines multiple stages of mass spectrometry to augment the selectivity and sensitivity of pesticide residue analysis. In MS/MS, analytes undergo ionization and fragmentation in the first stage of mass spectrometry. Selected ions are subsequently fragmented further in the second stage, yielding more precise and informative fragmentation patterns.

MS/MS confers several advantages for pesticide residue analysis. It enhances selectivity by enabling detection and quantification based on multiple transitions or specific fragment ions, thereby minimizing the likelihood of false positive or false negative results. Additionally, MS/MS offers heightened sensitivity compared to single-stage mass

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spectrometry, facilitating the detection of trace levels of pesticides in food samples.

Overall, MS/MS is a robust analytical tool that significantly enhances the accuracy and reliability of pesticide residue analysis, crucial for ensuring food safety and regulatory compliance.

2.4.4 High-Resolution Mass Spectrometry (HRMS)

High-resolution mass spectrometry (HRMS) is a technique that offers precise measurements of ion masses with high resolution. It is particularly valuable for analyzing complex samples that contain multiple pesticide residues. HRMS can be coupled with either gas chromatography (GC) or liquid chromatography (LC) to enhance the separation and identification of analytes [84].

HRMS provides several advantages for pesticide residue analysis. Firstly, it delivers accurate mass measurements, which enable determination of the elemental composition of analytes. This information is pivotal for identifying and confirming the presence of specific compounds. Secondly, HRMS offers high resolution, allowing for effective separation of analytes from matrix interferences. This capability enhances the reliability and accuracy of the analysis.

Moreover, HRMS is capable of non-targeted analysis, where complete mass spectra are acquired to detect and identify unknown compounds in food samples [85]. This versatility makes HRMS a powerful tool in pesticide residue analysis, supporting comprehensive and thorough assessments of food safety and regulatory compliance.

2.4.5 Ambient Mass Spectrometry

Ambient mass spectrometry represents a relatively recent advancement that facilitates direct analysis of samples without the need for extensive preparation or separation techniques. Techniques like direct analysis in real-time (DART) and desorption electrospray ionization (DESI) have proven effective for analyzing pesticide residues in various food matrices [86].

Ambient mass spectrometry offers several significant advantages for pesticide residue analysis. It eliminates time-consuming sample preparation steps, thereby reducing analysis time and costs. Furthermore, it allows for the analysis of samples in their natural state, preserving the integrity of the analytes. These techniques provide high sensitivity and selectivity, enabling the detection and quantification of trace levels of pesticides in complex matrices.

In summary, mass spectrometry methods such as GC-MS, LC-MS, MS/MS, HRMS, and ambient mass spectrometry are powerful tools for analyzing pesticide residues in food samples. They offer high sensitivity, selectivity, and the ability to provide detailed structural information about analytes. These techniques are indispensable for ensuring the safety and quality of food by facilitating the detection and quantification of pesticide residues, even at trace levels.

2.5 Immunoassay Techniques for Pesticide Residue Analysis

Immunoassay techniques have garnered considerable interest in pesticide residue analysis due to their notable attributes of high sensitivity, specificity, and user-friendliness. These methods rely on the specific interaction between an antibody and its corresponding target analyte, enabling accurate detection and quantification of pesticide residues across diverse food matrices [87].

2.5.1 Principle of Immunoassay Techniques

Immunoassay techniques operate on the principle of antigen-antibody interaction. Antibodies, proteins produced by the immune system in response to foreign substances (antigens), play a pivotal role. In pesticide residue analysis, pesticides serve as antigens, prompting the generation of specific antibodies that recognize and bind to these target pesticides.

Two primary types of immunoassay techniques are employed for pesticide residue analysis: enzyme-linked immunosorbent assay (ELISA) and immunochromatographic assays (ICA). Both methods capitalize on the precise binding between antibodies and pesticides to detect and quantify their presence in food samples [88].

2.5.2 Enzyme-Linked Immunosorbent Assay (ELISA)

ELISA (enzyme-linked immunosorbent assay) is a widely adopted immunoassay technique for analyzing pesticide residues in food. The process involves immobilizing antibodies on a solid support, typically a microplate. When a sample containing pesticide residues is added, the pesticide binds to the immobilized antibodies. Detection of the bound pesticide is achieved using an enzyme-labeled secondary antibody and a colorimetric substrate.

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ELISA offers several distinct advantages for pesticide residue analysis. Firstly, it boasts high sensitivity, capable of detecting pesticide residues at low concentrations in the parts per billion (ppb) range. ELISA kits are commercially available for a wide spectrum of pesticides, making them convenient and cost-effective for routine analysis. Moreover, ELISA procedures can be automated easily, facilitating high-throughput analysis of large sample sets.

Overall, ELISA is valued for its sensitivity, specificity, convenience, and scalability, rendering it an indispensable tool in the monitoring and assessment of pesticide residues in food.

2.5.3 Immunochromatographic Assays (ICA)

Immunochromatographic assays (ICAs), also known as lateral flow assays, are rapid and user-friendly immunoassay techniques employed for pesticide residue analysis. These assays operate on the principle of capillary action, where the sample migrates along a porous membrane containing immobilized antibodies. If the pesticide residue is present in the sample, it binds to the immobilized antibody, forming a visible colored line [89].

ICAs offer several advantages for pesticide residue analysis. They are straightforward to use, requiring minimal sample preparation and no specialized equipment. Results are typically obtained within minutes, making ICAs well-suited for on-site testing and rapid screening of large sample volumes. However, ICAs generally exhibit lower sensitivity compared to ELISA, with detection limits typically in the low parts per million (ppm) range.

Despite their lower sensitivity, ICAs are valued for their rapidity, simplicity, and suitability for field applications, making them a valuable tool for preliminary screening and quick assessment of pesticide residues in food samples.

2.5.4 Advantages and Limitations of Immunoassay Techniques

Immunoassay techniques offer several significant advantages for pesticide residue analysis. They are highly specific because antibodies are designed to selectively recognize and bind to the target pesticide. This specificity ensures accurate detection and quantification of pesticide residues, even in complex food matrices. Immunoassays are also rapid, delivering results within a short timeframe, which facilitates prompt decision-making in food safety.

Cost-effectiveness is another key advantage of immunoassay techniques. ELISA kits and immunochromatographic assays (ICAs) are commercially available at reasonable prices, making them accessible to laboratories with budget constraints. Furthermore, immunoassays can be easily automated, reducing manual labor and enhancing analytical efficiency.

However, immunoassay techniques have some limitations that warrant consideration. They rely on the availability of specific antibodies for each target pesticide, which restricts their applicability to known pesticides. Additionally, immunoassays may exhibit cross-reactivity, where antibodies bind to structurally similar compounds, potentially leading to false-positive results. Therefore, it is crucial to validate immunoassay methods and corroborate findings using validated techniques such as chromatography-mass spectrometry.

In summary, immunoassay techniques are valuable tools in pesticide residue analysis due to their specificity, rapidity, and cost-effectiveness. While they offer practical benefits, careful validation and complementary use with other analytical methods ensure reliable and accurate detection of pesticide residues in food samples.

2.5.5 Applications of Immunoassay Techniques in Pesticide Residue Analysis

Immunoassay techniques have become widely applied in pesticide residue analysis across diverse food commodities. They are frequently employed for the routine screening of large sample sets, enabling swift identification of samples that may exceed regulatory limits for pesticide residues.

These techniques are particularly advantageous in the initial stages of pesticide residue analysis, where rapid screening of numerous samples is necessary. Immunoassays serve as efficient preliminary screening tools, pinpointing samples that require further investigation using more specific and sensitive analytical methods.

Moreover, immunoassay techniques are pivotal for on-site testing and field monitoring of pesticide residues in food. Their simplicity and rapid turnaround time make them well-suited for deployment in remote locations or areas with limited laboratory infrastructure. Additionally, immunoassays have been instrumental in monitoring pesticide residues in organic food

production, where synthetic pesticide use is restricted [87, 90].

In conclusion, immunoassay techniques such as ELISA and immunochromatographic assays offer high sensitivity, specificity, and ease of use, rendering them invaluable for routine screening and rapid analysis of pesticide residues in food. However, to ensure accuracy and reliability, it is essential to validate immunoassay methods and verify results through confirmatory techniques, such as chromatography-mass spectrometry, when necessary. This comprehensive approach guarantees robust pesticide residue analysis, supporting food safety and regulatory compliance efforts effectively.

3 Sample Extraction and Cleanup Techniques

3.1 Solvent Extraction Techniques for Pesticide Residue Analysis

Solvent extraction is one of the most commonly used techniques for the extraction of pesticide residues from food samples. It is a simple and effective method that allows for the efficient extraction of a wide range of pesticides from various matrices. This technique involves the use of an organic solvent to dissolve the target analytes from the sample matrix, followed by separation and concentration of the analytes for further analysis.

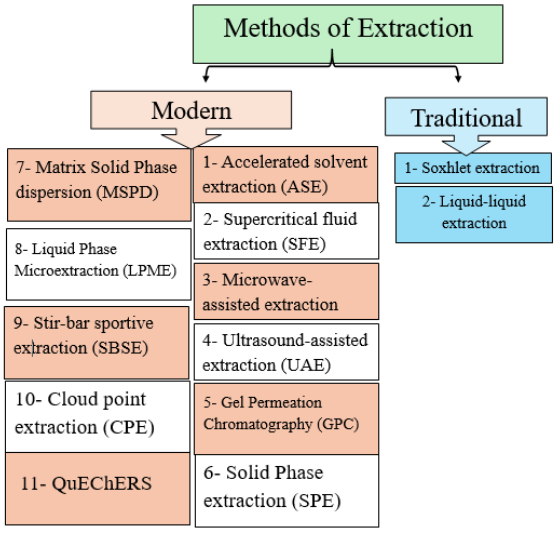

Fig. 2. The schematic diagram shows the various extraction methods.

3.1.1 Liquid-Liquid Extraction

Liquid-liquid extraction (LLE) is a well-established solvent extraction method widely used for isolating pesticide residues from food samples. In this technique, an organic solvent that is immiscible with water is employed to extract the target analytes from the aqueous sample matrix. The extraction process relies on the partitioning of analytes between the organic solvent phase and the aqueous phase. Subsequently, the organic phase, containing the extracted analytes, is separated and concentrated to facilitate further analysis [60].

LLE offers several advantages, including its simplicity, cost-effectiveness, and capability to extract a broad spectrum of pesticides efficiently. However, it also presents some drawbacks, such as the necessity for substantial quantities of organic solvents and the potential formation of emulsions during extraction. To mitigate these challenges, various modifications to the LLE method have been introduced. For instance, the addition of salt can enhance analyte partitioning, while techniques like dispersive liquid-liquid microextraction (DLLME) reduce the volume of organic solvents required [91].

These adaptations aim to enhance the efficiency and sustainability of LLE, making it a versatile and adaptable technique for pesticide residue extraction despite its initial limitations.

3.2. Solid-Phase Extraction

Solid-phase extraction (SPE) is a widely employed solvent extraction technique for isolating pesticide residues from food samples. In SPE, a solid sorbent material is utilized to selectively retain the target analytes from the sample matrix, while unwanted matrix components are washed away. The retained analytes are subsequently eluted from the sorbent using an organic solvent, and the resulting eluate is concentrated to facilitate further analysis [92].

SPE offers several advantages over liquid-liquid extraction (LLE). Firstly, it enables the selective retention of analytes and the removal of interfering matrix components, enhancing the purity of the extracted sample. Secondly, SPE employs smaller volumes of organic solvents compared to LLE, contributing to reduced solvent usage and environmental impact. Additionally, SPE can be automated, making the extraction process more efficient and reproducible across multiple samples.

However, SPE does present some limitations. One challenge is the potential for analyte loss during the elution step, which requires careful optimization of

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elution conditions to ensure maximum recovery. Furthermore, different classes of pesticides may require specific sorbent materials for optimal extraction efficiency, necessitating careful selection and validation of sorbents for each analyte group [93].

In summary, SPE is a versatile and efficient technique for pesticide residue extraction in food analysis. Its ability to selectively retain analytes, reduce solvent volumes, and automate the process makes it a preferred choice for laboratories aiming to achieve reliable and reproducible results in pesticide residue analysis.

3.2.1. Principles of Solid-Phase Extraction

Solid-phase extraction (SPE) relies on the principle of interaction between analytes and a solid-phase sorbent to extract pesticide residues from food samples effectively. Typically, the sorbent material, which can be silica-based or polymer-based, is packed into a cartridge or a disk. When the sample containing pesticide residues passes through the sorbent, the analytes of interest selectively interact with the sorbent and are retained, while unwanted matrix components are washed away. Subsequently, the retained analytes are eluted from the sorbent using an appropriate solvent, resulting in a concentrated extract suitable for direct analysis or further purification steps.

The retention of analytes on the solid-phase sorbent is governed by several mechanisms, including hydrophobic interactions, polar interactions, and ion exchange. Hydrophobic sorbents are typically used for extracting non-polar analytes, as they attract compounds with similar properties. For polar analytes, sorbents with polar functionalities or ion-exchange materials may be employed to facilitate retention and purification. The choice of sorbent depends on the specific physicochemical properties of the pesticide residues and the complexity of the sample matrix being analyzed.

In summary, SPE is a versatile extraction technique that offers selective retention of analytes, minimizes interference from matrix components, and allows for concentration of pesticide residues from food samples. By optimizing the choice of sorbent and elution conditions, SPE enhances the efficiency and reliability of pesticide residue analysis in various food matrices.

3.2.2 Types of Solid-Phase Extraction

There are several types of solid-phase extraction techniques that can be employed for pesticide residue analysis, depending on the specific requirements of the analysis. These include:

3.2.2.1 Bonded Silica Phases

Bonded silica phases are extensively employed in solid-phase extraction (SPE) because of their excellent selectivity and versatility in isolating pesticide residues from food samples. These phases are composed of silica particles that have been chemically modified with diverse functional groups, including C18 (octadecyl), C8 (octyl), and cyano groups. The selection of the bonded silica phase is guided by the polarity characteristics of the analytes and the complexity of the sample matrix.

C18 phases are particularly favored for extracting non-polar and moderately polar analytes from food matrices. The octadecyl functional group interacts strongly with hydrophobic compounds through hydrophobic interactions, facilitating their retention on the solid-phase sorbent during SPE. This makes C18 phases suitable for pesticides that exhibit these properties, ensuring effective extraction and concentration prior to analysis.

On the other hand, cyano phases are preferred for polar analytes due to their ability to interact via polar interactions. These phases can effectively retain polar compounds such as certain pesticides that require a more polar interaction for efficient extraction from the sample matrix.

In summary, the choice of bonded silica phase in SPE plays a critical role in optimizing the extraction efficiency and selectivity of pesticide residues in food samples. By selecting the appropriate phase based on the analyte's polarity characteristics and the composition of the food matrix, analysts can achieve reliable and accurate results in pesticide residue analysis.

3.2.2.2 Polymer-Based Phases

Polymer-based sorbents provide benefits, including excellent mechanical durability, resilience against pH variations, and the capability to extract a diverse array of analytes. These sorbents are commonly crafted from styrene-divinylbenzene copolymers or other polymeric resins. By introducing hydrophobic, polar, or ion-exchange functional groups, polymer-based phases can be customized to boost their specificity towards particular analytes.

3.2.2.3 Molecularly Imprinted Polymers

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Molecularly imprinted polymers (MIPs) are synthetic materials engineered to recognize and bind to particular target analytes selectively. They are synthesized by polymerizing functional monomers alongside the target analyte, acting as a template. After polymerization, the template is removed, leaving behind cavities within the polymer matrix that mirror the shape and characteristics of the target analyte. MIPs are renowned for their exceptional selectivity and find application in extracting a broad spectrum of analytes, including pesticides.

3.2.3 Procedure for Solid-Phase Extraction

The procedure for solid-phase extraction typically involves the following steps:

1. Conditioning: The solid-phase sorbent is conditioned with a suitable solvent to remove impurities and activate the sorbent. This step ensures that the sorbent is in an optimal state for analyte retention.
2. Sample Loading: The sample, either in liquid or solid form, is loaded onto the solid-phase sorbent. The sample matrix may need to be pre-treated to remove interfering compounds or to adjust the pH.
3. Washing: After the analytes are retained on the sorbent, the sorbent is washed with a solvent to remove any remaining matrix components and impurities. This step helps to improve the selectivity and purity of the analytes.
4. Elution: The retained analytes are eluted from the sorbent using a suitable solvent or solvent mixture. The elution solvent should be compatible with the subsequent analysis technique and should provide good recovery of the analytes.
5. Concentration: The eluate containing the analytes is evaporated or concentrated to reduce the volume and increase the analyte concentration. This step is particularly important when the analytes are present at low concentrations in the sample.

3.2.4 Advantages and Limitations of Solid-Phase Extraction

Solid-phase extraction offers several advantages over other extraction techniques in pesticide residue analysis. Some of the key advantages include:

- Selectivity: Solid-phase extraction allows for the selective extraction of target analytes while removing interfering compounds, resulting in cleaner extracts and improved analytical performance.
- Versatility: Solid-phase extraction can be used for a wide range of sample matrices, including fruits, vegetables, grains, meat, and dairy products. The technique can also be adapted for the extraction of different classes of pesticides, such as organochlorines, organophosphates, and pyrethroids.
- Concentration: Solid-phase extraction allows for the concentration of analytes, which is particularly useful when the analytes are present at low concentrations in the sample.
- Automation: Solid-phase extraction can be easily automated using commercially available systems, allowing for high-throughput analysis and improved reproducibility.

Despite its advantages, solid-phase extraction also has some limitations. These include:

- Matrix Effects: The presence of complex sample matrices can lead to matrix effects, which can affect the accuracy and precision of the analysis. Matrix effects can be minimized through proper sample preparation and the use of appropriate sorbents.
- Sample Throughput: Solid-phase extraction can be time-consuming, especially when processing large numbers of samples. However, the use of automated systems can help to improve sample throughput.
- Cost: Solid-phase extraction can be more expensive compared to other extraction techniques, primarily due to the cost of the sorbents. However, the benefits of improved selectivity and sensitivity often outweigh the cost considerations.

3.2.5 Applications of Solid-Phase Extraction in Pesticide Residue Analysis

Solid-phase extraction has found widespread applications in pesticide residue analysis across various food commodities. Some of the key applications include:

- Analysis of fruits and vegetables: Solid-phase extraction is commonly used for the pesticide residues analysis in fruits and vegetables, which are prone to contamination due to their direct exposure to pesticides during cultivation.

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- Analysis of grains and cereals: Solid-phase extraction is employed for the pesticide residues analysis in grains and cereals, which are staple food commodities and can be contaminated during cultivation, storage, and processing.
- Analysis of meat and poultry: Solid-phase extraction is used to analyze pesticide residues in meat and poultry products, which can be contaminated through the consumption of contaminated feed or environmental exposure.
- Analysis of dairy products: Solid-phase extraction is employed for the pesticide residue analysis in dairy products, such as milk and cheese, which can be contaminated through the consumption of contaminated feed or environmental exposure.
- Analysis of fish and seafood: Solid-phase extraction is used for the pesticide residues analysis in fish and seafood, which can be contaminated through environmental exposure.
- Analysis of processed foods: Solid-phase extraction is employed for the pesticide residues analysis in processed foods, such as canned fruits and vegetables, where the residues may be present as a result of processing or contamination during storage.

In conclusion, solid-phase extraction is a versatile and widely used technique in pesticide residue analysis. It offers several advantages, including selectivity, versatility, and the ability to concentrate analytes. Solid-phase extraction has found applications in various food commodities and can be used for the analysis of different classes of pesticides. Despite some limitations, solid-phase extraction remains an essential tool in the field of pesticide residue analysis.

3.3 Matrix Solid-Phase Dispersion Technique for Pesticide Residue Analysis

The matrix solid-phase dispersion (MSPD) technique is a sample preparation method that has gained popularity in recent years for the pesticide residues analysis in food. This technique offers several advantages over traditional extraction methods, such as simplicity, efficiency, and cost-effectiveness.

3.3.1 Principle of Matrix Solid-Phase Dispersion

The principle behind the Matrix Solid-Phase Dispersion (MSPD) technique involves dispersing the sample matrix with a solid-phase sorbent and subsequently eluting the target analytes from the sorbent for analysis. Initially, the sample matrix, whether solid or semi-solid, is homogenized with the solid-phase sorbent. The sorbent serves as a dispersing agent, aiding in the efficient extraction of target analytes from the matrix.

3.3.2 Procedure of Matrix Solid-Phase Dispersion

The MSPD technique involves several steps: sample preparation, dispersion, and elution.

1. Sample Preparation: This step includes grinding or milling the sample to achieve homogeneity. The homogenized sample is then mixed with a solid-phase sorbent, such as silica, alumina, or C18, and packed into a column or cartridge.
2. Dispersion: Here, a suitable solvent or solvent mixture is used to elute the target analytes from the sample matrix. As the solvent passes through the column, the analytes are retained by the sorbent while interfering matrix components are washed away.
3. Elution and Concentration: The analytes are then collected and concentrated for further analysis. This can be done by evaporating the solvent or using techniques like solid-phase microextraction (SPME) or solid-phase extraction (SPE). The concentrated analytes are subsequently analyzed using various methods, such as gas chromatography (GC) or liquid chromatography (LC) coupled with mass spectrometry (MS).

3.3.3 Advantages of Matrix Solid-Phase Dispersion

The MSPD technique offers several advantages for analyzing pesticide residues in food:

1. Simplicity and Minimal Sample Preparation: MSPD is a straightforward method that requires minimal sample preparation. The process of homogenizing the sample matrix with the solid-phase sorbent ensures representative sampling and minimizes the risk of analyte loss or degradation.
2. High Extraction Efficiency: MSPD is highly effective in extracting target analytes from complex matrices. The solid-phase sorbent selectively adsorbs the analytes, excluding interfering matrix components. This selectivity enhances both the sensitivity and accuracy of the analysis.
3. Cost-Effectiveness: The solid-phase sorbents used in MSPD are relatively inexpensive compared to

other extraction techniques like solid-phase extraction (SPE) or liquid-liquid extraction (LLE). Additionally, the simplicity of the MSPD technique reduces the need for specialized equipment, further lowering costs.

4. Versatility: MSPD is versatile and can be applied to a wide range of sample matrices, including fruits, vegetables, grains, meat, and dairy products. It is suitable for analyzing both polar and non-polar pesticides, making it applicable to various pesticide residue analysis needs.

3.3.4 Limitations of Matrix Solid-Phase Dispersion

Despite its advantages, the MSPD technique has some limitations:

1. Matrix Effects: One limitation is the potential for matrix effects, where co-extracted components from the sample matrix can interfere with the analysis. These components may suppress or enhance the ionization of the analytes during analysis, affecting the accuracy of the results.
2. Limited Sorbent Capacity: The solid-phase sorbent used in MSPD has a limited capacity, allowing for only small sample sizes to be processed at a time. This can be problematic for highly contaminated samples, potentially requiring larger sample sizes or multiple extractions.
3. Unsuitability for Volatile or Thermally Labile Pesticides: The MSPD technique may not be suitable for analyzing volatile or thermally labile pesticides, as the elution step can lead to analyte loss or degradation. For such cases, alternative extraction techniques like headspace analysis or thermal desorption may be more appropriate.

3.3.5 Applications of Matrix Solid-Phase Dispersion

The MSPD technique has been successfully applied to a variety of food matrices for pesticide residue analysis, including fruits, vegetables, grains, meat, dairy products, and processed foods. Its simplicity and efficiency make it a valuable tool for routine analysis in food safety laboratories.

In conclusion, matrix solid-phase dispersion (MSPD) is a straightforward, efficient, and cost-effective method for analyzing pesticide residues in food. It offers several advantages over traditional extraction techniques, such as simplicity, efficiency, and versatility. Despite some limitations, MSPD has found widespread application in food safety analysis and remains an important tool for detecting pesticide residues in food.

3.4 QuEChERS Technique

The QuEChERS (Quick, Easy, Cheap, Effective, Rugged, and Safe) technique is a modern solvent extraction method widely adopted for analyzing pesticide residues in food samples. This method combines aspects of both liquid-liquid extraction and solid-phase extraction in a multi-step process. Initially, an extraction solvent such as acetonitrile or methanol is added to the sample matrix, followed by the addition of salts to enhance the partitioning of analytes. The sample is then homogenized and centrifuged to separate the organic phase containing the extracted analytes from the aqueous phase.

QuEChERS (Quick, Easy, Cheap, Effective, Rugged, and Safe) is a highly regarded solvent extraction method in pesticide residue analysis for food samples. This approach incorporates dispersive solid-phase extraction (dSPE) to enhance the purity of the organic phase by removing interfering matrix components before subsequent analysis. QuEChERS is valued for its simplicity, speed, and ability to extract a broad spectrum of pesticides from diverse food matrices. It minimizes the use of organic solvents compared to traditional methods, contributing to environmental sustainability. The integration of dSPE improves the selectivity and sensitivity of the analysis, ensuring reliable results in pesticide residue quantification. Regulatory agencies and laboratories worldwide widely adopt QuEChERS for its robust performance in pesticide residue analysis in food samples.[94, 95].

In summary, solvent extraction techniques like liquid-liquid extraction, solid-phase extraction, and the QuEChERS method are pivotal in analyzing pesticide residues in food samples. These methods facilitate effective and selective extraction of diverse pesticides from different matrices. The selection of a solvent extraction technique hinges on considerations such as the analyte characteristics, complexity of the sample matrix, and the desired sensitivity and selectivity of the analysis. Each technique offers distinct advantages suited to varying analytical needs, ensuring reliable detection and quantification of pesticide residues in food samples.

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3.4.1 QuEChERS Technique for Pesticide Residue Analysis

The QuEChERS (Quick, Easy, Cheap, Effective, Rugged, and Safe) technique is a widely adopted method for the extraction and cleanup of pesticide residues in food samples. Developed in the early 2000s, it provides an efficient alternative to traditional extraction methods like liquid-liquid extraction and solid-phase extraction, which are often time-consuming and require large quantities of organic solvents. QuEChERS is known for its simplicity, speed, and cost-effectiveness, making it a popular choice for pesticide residue analysis in various food matrices.

3.4.2 Principle of the QuEChERS Technique

The QuEChERS technique comprises two primary steps: extraction and cleanup. During the extraction step, pesticide residues from the food matrix are extracted using a mixture of acetonitrile and water, along with salts to enhance analyte partitioning into the organic phase. This extraction process typically involves vigorous shaking of the sample for a few minutes. After extraction, the sample undergoes centrifugation to separate the organic phase (containing the analytes) from the aqueous phase.

Subsequently, in the cleanup step, dispersive solid-phase extraction (dSPE) is employed to eliminate unwanted matrix components and co-extracted interferences. This involves adding a blend of sorbents, such as primary secondary amine (PSA) and C18, to the extract. These sorbents selectively retain interfering compounds while allowing the pesticide residues to pass through. The cleanup procedure concludes with centrifugation to separate the sorbents from the solution containing the analytes.

3.4.3 Advantages of the QuEChERS Technique

The QuEChERS technique provides several advantages over traditional extraction methods used for pesticide residue analysis. Firstly, it minimizes the need for extensive sample preparation, thereby reducing the time and effort required for analysis. This simplicity also enhances its accessibility to laboratories with limited resources. Moreover, the QuEChERS technique utilizes smaller quantities of organic solvents compared to conventional methods, contributing to its environmental friendliness.

Another significant advantage of the QuEChERS technique is its versatility across various food matrices. It is applicable to a wide range of samples including fruits, vegetables, grains, meat, poultry, dairy products, and seafood. The method has been effectively employed for analyzing diverse classes of pesticides such as organochlorines, organophosphates, carbamates, pyrethroids, and neonicotinoids. Furthermore, the QuEChERS approach can be easily adapted to accommodate different sample sizes, facilitating the analysis of both small and large volumes of samples.

3.4.4 Methodology and Procedure

The QuEChERS technique involves a series of steps that need to be followed carefully to ensure accurate and reliable results. The general procedure for the QuEChERS technique is as follows:

1. Weigh the food sample and homogenize it to obtain a representative subsample.
2. Add an appropriate amount of water to the sample to achieve the desired sample-to-solvent ratio.
3. Add salts, such as magnesium sulfate and sodium chloride, to enhance the partitioning of the analytes into the organic phase.
4. Add acetonitrile to the sample to extract the pesticide residues.
5. Shake the sample vigorously for a few minutes to facilitate the extraction.
6. Centrifuge the sample to separate the organic phase from the aqueous phase.
7. Transfer the organic phase to a clean tube.
8. Add the cleanup sorbents, such as PSA and C18, to the extract.
9. Shake the sample again to allow the sorbents to selectively retain interfering compounds.
10. Centrifuge the sample to separate the sorbents from the analyte-containing solution.
11. Transfer the cleaned extract to a vial for analysis.

3.4.5Analytical Techniques Compatible with QuEChERS

The QuEChERS technique is compatible with a wide range of analytical methods used in pesticide residue analysis, including gas chromatography (GC) and liquid chromatography (LC), often coupled with detectors such as mass spectrometry (MS) and tandem mass spectrometry (MS/MS). GC-MS and LC-MS/MS are particularly favored due to their high sensitivity and specificity.

The selection of an analytical technique depends on several factors specific to the analysis, such as the

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characteristics of the target analytes, required detection limits, and compliance with regulatory standards. GC-MS is typically preferred for volatile and semi-volatile compounds because of its effective separation and detection capabilities for these substances. Conversely, LC-MS/MS is well-suited for polar and non-volatile compounds, offering robust separation and identification abilities.

Both GC-MS and LC-MS/MS methodologies enable accurate quantification of pesticide residues in food samples, ensuring precise assessment and adherence to safety regulations. These techniques are vital in safeguarding food safety by reliably detecting even trace amounts of pesticides in diverse food matrices.

3.4.6 Limitations and Challenges

While the QuEChERS technique has significantly advanced pesticide residue analysis, it faces several limitations and challenges that warrant consideration. One primary concern is the potential for matrix effects, which can cause ion suppression or enhancement in the analytical signal, thereby impacting the accuracy and precision of results. Mitigating strategies are essential to minimize these effects during analysis.

Another challenge lies in the variability of extraction efficiency within the QuEChERS technique. This variability can arise due to differences in analyte characteristics and interactions with diverse food matrices. Certain pesticides may exhibit lower recovery rates due to their chemical properties or specific interactions with matrix components. Consequently, thorough method validation tailored to each analyte and food matrix is crucial to ensure reliable analytical outcomes.

Additionally, the QuEChERS method may not be suitable for analyzing certain pesticide classes, such as highly polar or thermally labile compounds. In such instances, alternative extraction and cleanup methods must be considered to ensure effective detection and quantification.

Nevertheless, despite these challenges, the QuEChERS technique remains highly valued for pesticide residue analysis in food due to its simplicity, rapidity, and cost-effectiveness. It is widely adopted in laboratories worldwide for routine testing. As analytical techniques continue to advance and new sorbents are developed, ongoing improvements in the QuEChERS approach are anticipated, further enhancing its applicability and reliability in food safety testing.

3.5 Supercritical Fluid Extraction Techniques for Pesticide Residue Analysis

Supercritical fluid extraction (SFE) has garnered considerable interest in recent years for the analysis of pesticide residues in food. This technique employs supercritical fluids, typically carbon dioxide (CO2), as the extraction solvent to selectively extract target analytes from complex matrices. Compared to traditional extraction methods, SFE boasts several advantages, such as high selectivity, minimal sample preparation requirements, and low solvent consumption.[96].

3.5.1 Principle of Supercritical Fluid Extraction

Supercritical fluids refer to substances that are above their critical temperature and pressure, where they exhibit unique properties advantageous for extraction purposes. Carbon dioxide (CO_2), for example, becomes a supercritical fluid at temperatures above 31.1°C and pressures above 73.8 bar. In this state, CO_2 behaves both like a liquid and a gas, enabling it to permeate solid matrices and dissolve analytes of interest.

The principle of supercritical fluid extraction (SFE) involves utilizing CO_2 as the extraction solvent. CO2 is introduced into a high-pressure extraction vessel containing the sample matrix. It is then heated to its supercritical state, allowing it to penetrate the sample and dissolve the target analytes. The dissolved analytes are subsequently carried out of the extraction vessel and collected for further analysis.

3.5.2 Advantages of Supercritical Fluid Extraction

Supercritical fluid extraction offers several advantages over traditional extraction techniques for pesticide residue analysis in food. Some of the key advantages include:

1. Selectivity: CO_2 can be easily modified by adjusting the temperature and pressure, allowing for selective extraction of target analytes while leaving unwanted matrix components behind. This selectivity is crucial for accurate and reliable pesticide residues analysis in complex food matrices.
2. Minimal sample preparation: SFE requires minimal sample preparation compared to other extraction techniques. Since CO_2 is a nonpolar

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solvent, it can extract analytes directly from the sample matrix without the need for extensive cleanup steps. This reduces the risk of analyte loss or contamination during sample preparation.

3. Low solvent consumption: SFE utilizes CO_2 as the extraction solvent, which is non-toxic, non-flammable, and readily available. Unlike traditional organic solvents, CO_2 can be easily recovered and reused, resulting in significant cost savings and reduced environmental impact.
4. Rapid extraction: Supercritical fluid extraction is a relatively fast technique compared to other extraction methods. The high diffusivity of supercritical fluids allows for efficient extraction of analytes from the sample matrix, reducing the overall extraction time.
5. Compatibility with analytical techniques: The extracts obtained from SFE can be directly analyzed using various analytical techniques, such as gas chromatography (GC) or liquid chromatography (LC), coupled with mass spectrometry (MS). This compatibility allows for seamless integration of SFE into existing analytical workflows.

3.5.3 Applications of Supercritical Fluid Extraction in Pesticide Residue Analysis

Supercritical fluid extraction has found numerous applications in the pesticide residues analysis in various food matrices[33, 45, 96, 97]. Some of the common applications include:

1. Fruits and vegetables: SFE has been successfully used for the extraction of pesticide residues from fruits and vegetables. The selectivity of CO2 allows for the extraction of target analytes while minimizing interference from complex matrix components, such as pigments and sugars.
2. Grains and cereals: Supercritical fluid extraction has been employed for the pesticide residues analysis in grains and cereals. The ability of CO2 to penetrate the solid matrix and selectively extract analytes makes it an ideal technique for these complex matrices.
3. Meat and poultry: SFE has been utilized for the extraction of pesticide residues from meat and poultry samples. The high selectivity of CO2 ensures the extraction of target analytes while minimizing the extraction of unwanted components, such as fats and proteins.
4. Dairy products: Supercritical fluid extraction has been applied to the pesticide residues analysis in dairy products, including milk and cheese. The compatibility of CO2 extracts with various analytical techniques allows for accurate and reliable pesticide residues analysis in these matrices.
5. Fish and seafood: SFE has been used for the extraction of pesticide residues from fish and seafood samples. The ability of CO2 to penetrate the lipid-rich matrices of fish and seafood allows for efficient extraction of target analytes.

3.5.4 Challenges and Limitations of Supercritical Fluid Extraction

While supercritical fluid extraction offers several advantages, it also has some challenges and limitations that need to be considered. These include:

1. Limited analyte solubility: Not all pesticide residues are soluble in supercritical CO2, which can limit the applicability of SFE for certain analytes. However, the addition of co-solvents or modifiers can enhance the solubility of analytes and overcome this limitation.
2. Matrix effects: Complex food matrices can contain various interfering components, such as pigments, sugars, and fats, which can affect the extraction efficiency and selectivity of SFE. Proper optimization of extraction conditions and the use of appropriate modifiers can help mitigate these matrix effects.
3. Equipment cost: The setup and maintenance of supercritical fluid extraction equipment can be costly compared to traditional extraction methods. However, the long-term cost savings from reduced solvent consumption and improved efficiency can offset these initial costs.
4. Method development: The optimization of extraction conditions, including temperature, pressure, and modifier concentration, can be time-consuming and require extensive method development. However, once optimized, the method can be easily replicated for routine analysis.

Despite these challenges, supercritical fluid extraction has proven to be a valuable technique for the pesticide residues analysis in food. Its unique properties and advantages make it an attractive alternative to traditional extraction methods, offering improved

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selectivity, reduced solvent consumption, and simplified sample preparation. As the field of pesticide residue analysis continues to evolve, SFE is expected to play a significant role in advancing analytical capabilities and ensuring food safety.

3.6 Other Extraction and Cleanup Techniques for Pesticide Residue Analysis

Besides the extraction and cleanup methods commonly discussed earlier, numerous other techniques exist for analyzing pesticide residues in food. These methods offer diverse approaches to sample preparation, offering researchers and analysts a variety of choices tailored to their specific analytical needs.

3.6.1 Solid-Phase Microextraction (SPME)

Solid-phase microextraction (SPME) has become increasingly popular for analyzing pesticide residues in food due to its solvent-free extraction method. SPME involves using a fiber coated with a stationary phase that selectively adsorbs target analytes from the sample matrix. Subsequently, the fiber is desorbed in the injection port of a gas chromatograph (GC) or liquid chromatograph (LC) coupled with a mass spectrometer (MS) for analysis.

SPME offers several advantages over traditional extraction techniques. It eliminates the need for large volumes of organic solvents, thereby reducing both the cost and environmental impact of the analysis. SPME also facilitates rapid extraction times and allows for the simultaneous extraction of multiple analytes. However, it's worth noting that SPME may not be universally applicable to all types of pesticides, as some compounds may not be efficiently extracted using this method [98, 99].

3.6.2 Stir Bar Sorptive Extraction (SBSE)

Stir bar sorptive extraction (SBSE) is a solvent-free extraction technique extensively employed for analyzing pesticide residues in food. This method utilizes a stir bar coated with a sorbent material, which is submerged in the sample matrix for a specified duration to facilitate the extraction of target analytes. Subsequently, the stir bar is desorbed in an appropriate solvent and subjected to analysis using GC or LC-MS [100-102].

SBSE presents numerous advantages over traditional extraction methods. It achieves high extraction efficiencies, enabling the retrieval of a broad spectrum of analytes encompassing both polar and non-polar compounds. SBSE also ensures exceptional sensitivity and reproducibility, thereby establishing itself as a valuable technique for analyzing pesticide residues in intricate food matrices [103, 104].

3.6.3 Dispersive Liquid-Liquid Microextraction (DLLME)

Dispersive liquid-liquid microextraction (DLLME) is a simple and efficient extraction technique that has been widely used for the pesticide residues analysis in food [105]. DLLME involves the dispersion of a small volume of an extraction solvent into the sample matrix, followed by the addition of a dispersing solvent to form a cloudy solution. The target analytes are then extracted into the fine droplets of the extraction solvent, which are subsequently separated and analyzed using GC or LC-MS [106].

DLLME offers several advantages over traditional extraction techniques. It requires small volumes of organic solvents, reducing both the cost and the environmental impact of the analysis. DLLME also provides rapid extraction times and high extraction efficiencies, making it a suitable technique for the pesticide residues analysis in a wide range of food matrices [107].

3.6.4 Pressurized Liquid Extraction (PLE)

Pressurized liquid extraction (PLE), also referred to as accelerated solvent extraction (ASE), utilizes elevated temperatures and pressures to extract analytes from solid or semi-solid samples. In PLE, a pressurized solvent is employed to pass through the sample matrix, effectively extracting the target analytes[108]. The extract is then collected and analyzed using GC or LC-MS. Pressurized liquid extraction (PLE) offers numerous advantages compared to traditional extraction methods. It facilitates rapid extraction times and high extraction efficiencies, enabling the analysis of a large number of samples within a short timeframe. PLE is versatile in extracting a wide range of analytes, encompassing both polar and non-polar compounds.
However, it's essential to recognize that PLE necessitates specialized equipment and may not be universally suitable for all types of food matrices.[109].

3.6.5 Microwave-Assisted Extraction (MAE)

Microwave-assisted extraction (MAE) is a technique that uses microwave irradiation to heat the sample matrix and facilitate the extraction of analytes. MAE

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involves the use of a microwave reactor, in which the sample matrix is placed along with a suitable extraction solvent[110]. The microwave energy rapidly heats the sample, promoting the release of the target analytes into the solvent. The extract is then collected and analyzed using GC or LC-MS [111, 112].

Microwave-assisted extraction (MAE) offers several advantages compared to traditional extraction techniques. It accelerates extraction processes, yielding rapid extraction times and high efficiencies, which facilitate the analysis of numerous samples within a short timeframe. MAE is versatile, capable of extracting a wide array of analytes spanning both polar and non-polar compounds. However, it necessitates specialized equipment and may not be universally suitable for all food matrices [113].

In summary, numerous extraction and cleanup techniques are accessible for analyzing pesticide residues in food. These methods present diverse approaches to sample preparation, granting researchers and analysts a spectrum of choices to suit their analysis needs. Careful consideration of factors such as the target analytes, food matrix characteristics, and desired sensitivity and selectivity is crucial in selecting the most suitable technique. This ensures accurate and reliable pesticide residue analysis in food samples.

4 Method Validation and Quality Assurance

4.1 Validation Parameters for Pesticide Residue Analysis

Validation of analytical methods is a crucial step in pesticide residue analysis to ensure the accuracy, reliability, and reproducibility of the results. It involves evaluating various parameters to determine the method's performance characteristics. These validation parameters provide information about the method's suitability for its intended purpose and help establish its credibility. In this section, we will discuss the key validation parameters for pesticide residue analysis.

Selectivity

Selectivity refers to the analytical method's ability to differentiate the analyte of interest from other components present in the sample matrix. In pesticide residue analysis, selectivity is essential to avoid interference from matrix components that may affect the accuracy of the results. Selectivity can be evaluated by analyzing blank samples and determining the presence of any interfering peaks or signals that may overlap with the analyte peak. The absence of interfering peaks ensures the method's selectivity for the target analyte.

Linearity

Linearity is the ability of the analytical method to produce results that are directly proportional to the concentration of the analyte in the sample. It is important to establish linearity to accurately quantify the pesticide residues present in food samples. Linearity can be assessed by analyzing a series of standard solutions with known concentrations of the analyte and plotting a calibration curve. The linearity of the method is determined by the correlation coefficient (R^2) of the calibration curve, which should be close to 1.

Sensitivity

Sensitivity refers to the ability of the analytical method to detect and quantify low levels of pesticide residues in food samples. It is determined by the limit of detection (LOD) and limit of quantification (LOQ) of the method. The LOD is the lowest concentration of the analyte that can be reliably detected, while the LOQ is the lowest concentration that can be quantified with acceptable accuracy and precision. Sensitivity is crucial in pesticide residue analysis, as regulatory limits for pesticide residues are often set at very low levels.

Accuracy

Accuracy in analytical chemistry refers to how close the measured value is to the true value of the analyte concentration. It is typically assessed by analyzing spiked samples with known concentrations of the analyte and comparing the measured values against the expected values. Accuracy is often expressed as recovery, calculated as the ratio of the measured concentration to the spiked concentration multiplied by 100%.

An acceptable recovery range is usually set between 70% and 120%. This range indicates that the method is accurate in quantifying pesticide residues in food samples, as it demonstrates that the measured values are close to the true concentrations of the analyte.

Precision

Precision in an analytical method refers to its ability to produce consistent and reproducible results. This is evaluated by analyzing replicate samples and calculating the relative standard deviation (RSD) of the measurements. Precision can be assessed at various levels, including repeatability (intra-day precision) and intermediate precision (inter-day precision).

Repeatability is determined by analyzing multiple aliquots of the same sample within a single day, while intermediate precision involves analyzing the same sample across different days or by different analysts. Low RSD values indicate high precision and reliability of the analytical method.

Robustness

Robustness refers to the capability of an analytical method to withstand minor variations in experimental conditions without significant impact on results. This is assessed by intentionally introducing slight changes in parameters like pH, temperature, extraction time, or mobile phase composition, and observing their effects on outcomes. Conducting robustness studies helps identify key parameters that might influence the method's performance and ensures its reliability under typical laboratory conditions.

Matrix effects refer to the interference caused by the sample matrix on the analyte's ionization or detection in an analytical method. In pesticide residue analysis, matrix effects can lead to signal suppression or enhancement, impacting the accuracy and precision of the results. These effects can be assessed by comparing the analyte's response in a neat solvent to its response in the presence of the sample matrix. Techniques such as matrix-matched calibration or the use of internal standards can help mitigate matrix effects.

Method Specificity

Method specificity refers to the ability of the analytical method to accurately identify and quantify the target analyte in the presence of other compounds that may be present in the sample matrix. It is important to ensure that the method is specific to the analyte of interest and does not produce false-positive or false-negative results. Specificity can be assessed by analyzing blank samples and determining the absence of any interfering peaks or signals that may interfere with the analyte's detection.

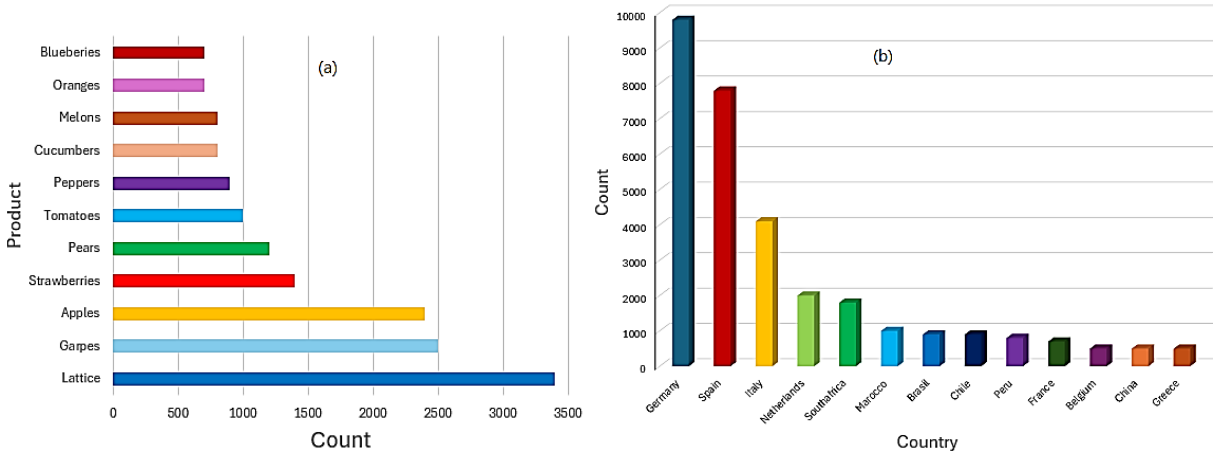

Fig. 3. The bar plots (a) the most represented fruits and vegetables, and (b) the most represented countries.

Stability

Stability pertains to the capacity of the analyte to remain unchanged throughout sample storage and analysis. It is crucial to ensure that pesticide residues in food samples do not degrade or undergo chemical transformations during analytical processes. Evaluating stability involves analyzing replicate samples stored under various conditions (e.g., refrigerated, frozen) and comparing the results. Consistency in measured concentrations across different storage conditions indicates the analyte's stability during sample handling and analysis.

Matrix Effects

5 Applications of Pesticide Residue Analysis

5.1 Pesticide Residue Analysis in Fruits and Vegetables

Fruits and vegetables are integral components of a nutritious diet, providing essential vitamins, minerals, and dietary fiber. Despite their nutritional benefits, they are susceptible to pesticide contamination due to the routine application of pesticides intended to protect crops from pests and diseases [114]. Pesticide residues

IJMTI vol. 4, issue 1 (2024) 42-74 https://doi.org/10.21608/IJMTI.2024.298332.1105

in fruits and vegetables can pose a risk to consumer health if they exceed the maximum residue limits (MRLs) established by regulatory authorities.

Therefore, it is crucial to analyze and monitor pesticide levels in these food items to maintain food safety standards and comply with regulations. As detailed in Table 1, various extraction and pre-treatment techniques are used to detect pesticide residues in fruits and vegetables. However, there is no universally accepted standard method for pesticide extraction in laboratories.

5.2 Dataset of pesticide residue analysis

The pesticides featured in the dataset are used under various climatic conditions. The analysis results are presented in Figures 3a and 3b. In Figure 3a, eleven fruits and vegetables are depicted, with an overall equal distribution between the two categories. Tomatoes are the third most prevalent vegetable, with a count of 1,023. Grapes are the most prevalent fruit, with a total count of 2,500, closely followed by apples with 2,369 counts. Strawberries and pears follow with counts of 1,372 and 1,148, respectively, while the remaining instances are around 600 counts each. Figure 3b shows the most represented countries in the dataset. Germany leads with 9,813 counts, followed by Spain with 7,841 counts, and Italy with 4,009 counts. Most other countries have counts well below the 1,000 mark.

5.3 Concentrations of pesticides and residue patterns detected in some crops.

Pesticides are applied to crop plants to protect them from pests to achieve higher yields. The dosage and methods of application vary based on the principles adopted, which differ among countries. Food safety regulations in each country directly influence these application principles. While the presence of pesticide residues in the harvested crops is inevitable, it must not exceed the approved limits.

Figure 4 illustrates the number of residues detected in each commodity. According to Fig. 4, grapes exhibited the highest number of residues, followed by strawberries, dried apricots, dried figs, peaches, pomegranates, cherries, peppers, tomatoes, pears, nectarines, quinces, olives, fresh apricots, apples, and tangerines.

6 Future Perspectives in Pesticide Residue Analysis

Pesticide residue analysis is pivotal for safeguarding the safety and quality of our food. With ongoing technological advancements, the development of new Analytical techniques aims to enhance the precision, sensitivity, and efficiency of pesticide residue analysis. This section delves into future perspectives in pesticide residue analysis and their potential impact on the field in the years ahead.

6.1 Advancements in Analytical Techniques

Advancements in analytical techniques have the potential to revolutionize pesticide residue analysis by addressing existing challenges and improving overall efficiency. Traditional methods like gas chromatography (GC) and liquid chromatography (LC) coupled with mass spectrometry (MS) have been effective but are often hindered by lengthy sample preparation and limited sensitivity.

One promising innovation is ambient ionization mass spectrometry (AIMS), which enables direct sample analysis without extensive preparation. AIMS has the capacity to significantly reduce analysis time and increase throughput in pesticide residue detection.

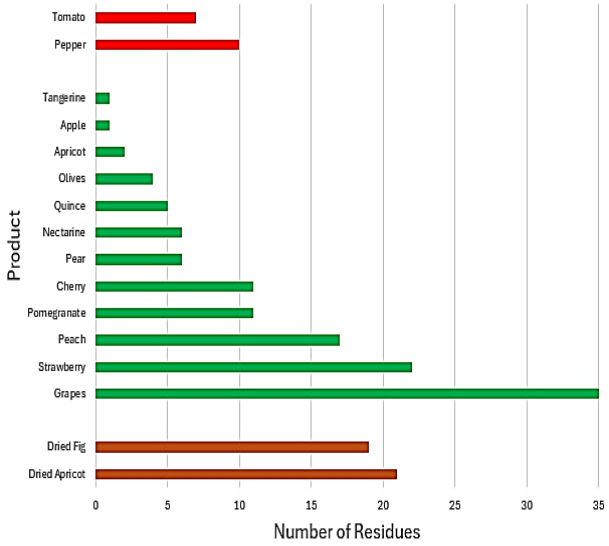

Fig. 4 Number of pesticide residues in each crop.

Table 1 Summary of the extraction and pre-treatment methods for the estimation of pesticide residues in vegetables and fruits [114].

Extraction method	Matrix	Study country	Class of pesticide (s)	Recovery (%)	Ref.
Liquid-liquid extraction (LLE)	Apples, broccoli, cherries, cucumbers, grapes, papayas, pears, tamarillos, tomatoes.	Germany	Dithiocarbamate fungicide (DMDs, EBDs and PBDs)	97–101	[115]
	Apricot, cherry, cucumber, grape, peach, pepper, spinach, tomato, zucchini.	Turkey	Mult. Pets.	70–120	[116]
	Beans green	Egypt	Mult. Pets.	90–110	[117]
	Bean sprouts	Republic of Korea	Fungicide and plant growth regulator	80.4–96.3	[118]
	Banana, cucumber, grapefruit, orange, pepper, strawberry, tomato.	Belgium	Mult. Pets.	70–110	[119]
Solid phase extraction (SPE)	Rape, cauliflower and leek	China	OPPs (trichlorfon and monocrotophos)	88.5–94.2	[120]
	Peaches, lettuce and wheat grain	Bulgaria	Mult. Pets.	73–117	[121]
	Papaya	Brazil	Mult. Pets.	91–105	[122].
	Berry fruits, rasberry, strawberry, blueberry and grape	China	Mult. Pets.	63–137	[123]
	Cucumber, cabbage, cole and capsicum	China	Mult. Pets.	< 70	[124]
	Brinjal, cabbage, cauliflower, guava, okra, onion, Apple, banana, grape, mango, orange, pomegranate, potato.	India	Mult. Pets.	74–111	[125]
	Apple, cabbage, chicken, egg, milk, pork, potato, rice, tea.	China	Neonicotinoid pesticide	65–120	[126]
Solid phase microextraction (SPME)	Apple, cabbage, cucumber, tomato.	Malaysia	Mult. Pets.	73–118	[127]
	Strawberry and Cucumber	Malaysia	OPPS and OCPs	77.3–91	[128]
	Cabbage, cucumber, peach.	China	Pyrethroid	85–103.5	[129]
Matrix solid phase dispersion (MSPD)	Apple, grape, strawberry, tomato, cabbage, spinach, rape and banana	China	OPPs	71.2–102.8	[130]
	Cucumber and orange Almeria,	Spain	Mult. Pets.	70–110	[131]

Quick, easy, cheap, effective, rugged, and safe method (QuEChERS)	Tomato, apple and green-beans	Austria	Mult. Pets.	93	[132]
	Apple, tomatoes, carrot, oranges and olives	Spain	Mult. Pets.	70–120	[133]
	Lettuce, cabbage and leek,	Poland	Mult. Pets.	70–120	[134]
	Grape	Brazil	Mult. Pets.	70–125	[135]
	Pomegranate, cauliflower, cabbage, arugula, cucumber, lemon and grape	Turkey	Mult. Pets.	70–120	[136]
	Apple, oranges, strawberry, plum and lettuce	Slovak Republic	Mult. Pets.	70–110	[137]
	Tomato, bell pepper, eggplant, cucumber, zucchini, cabbage, carrot, potato, strawberry, watermelon, apple and grapes	Kuwait	Mult. Pets.	85–106	[138]
	Tomato	Brazil	Mult. Pets.	70–120	[139]
	Spinach and cauliflower	China	Mult. Pets.	43–103	[140]
	Strawberries, plums, carrots, green peppers, milk, molasses, alfalfa oats, corn silage, dry pet food, soybean, almonds and foliage	USA	Mult. Pets.	70–120	[141]
	Potato, cowpea, corn, wheat and rice	China	Pyrazole (Penflufen)	76.1–101	[142]
	Banana	Brazil	Mult. Pets.	70–120	[143]
	Rice, corn, cucumbers, tomatoes, apples, and bananas	China	Mult. Pets.	70–120	[144]
	Potato, cabbage, cauliflower, carrot, garlic, broccoli, leek, celery, ginger, peas, lettuce, peach, plum, pear, baby apple, strawberry and passion fruits	India	Organophosphate pesticide	76.8–110.30	[145]
Other extraction methods Gel permeation chromatography (GPC)	Oranges, apples, peaches, pears, grapefruits, lettuce, tomato, cabbage, potato, onion and leek	Croatia	Mult. Pets.	Not stated	[146]

Liquid-liquid microextraction (LLME)	Fruits and fruit juices	Iran	Pyrethroid insecticides	73–92	[147]
Capillary electrophoresis (CE)	Tomato	China	OPPs	88.7–96.1	[148]
	Kidney beans and cucumber	China	OPPs	78.8–106.3	[149]

- DMDs: dimethyldithiocarbomates; EBDs: ethylenebisdithiocarbomate; OPPs: Organophosphorus pesticides; OCPs: Organochlorine pesticides; PBDs: porpylenebis dithiocarbomate, Mult. Pets.: Multiclass pesticides

Another area of advancement involves the integration of nanomaterials into pesticide residue analysis. Nanomaterials offer unique properties that can enhance the sensitivity and selectivity of analytical methods. For instance, nanoparticles can serve as efficient sorbents in solid-phase extraction (SPE), thereby improving the extraction efficiency of pesticide residues. Moreover, nanomaterials can act as labels in immunoassay techniques, enabling the detection of pesticide residues at lower concentrations.

These innovations hold promise for overcoming current limitations in pesticide residue analysis, paving the way for more efficient, sensitive, and reliable methods in the future.

6.2 New Extraction and Cleanup Techniques

Sample extraction and cleanup are crucial stages in pesticide residue analysis, traditionally managed through techniques like solvent extraction and solid-phase extraction (SPE). Although effective, these methods can be labor-intensive and require large amounts of organic solvents.

Recently, there has been a growing interest in greener extraction and cleanup methods. One significant advancement is supercritical fluid extraction (SFE), which uses supercritical fluids such as carbon dioxide to extract pesticide residues from food samples. SFE offers numerous benefits, including reduced solvent use, shorter extraction times, and the ability to extract a wide range of pesticide classes.

Another emerging technique is the use of molecularly imprinted polymers (MIPs) for sample cleanup. MIPs are synthetic materials designed to selectively bind specific analytes and can be used as sorbents in SPE or as stationary phases in chromatography. MIPs offer several advantages over traditional cleanup methods, including exceptional selectivity, robustness, and reusability. These innovations represent significant progress in improving the efficiency and sustainability of pesticide residue analysis in food samples.

6.3 Rapid Screening Methods

Rapid screening methods are essential for the initial assessment of pesticide residues in food samples. Traditionally, enzyme-linked immunosorbent assays (ELISAs) have been widely used for this purpose. However, ELISAs may not always meet the required sensitivity and specificity standards.

An emerging rapid screening method is the use of biosensors. Biosensors are analytical devices that combine a biological recognition element with a transducer to detect and quantify analytes. They offer several advantages, including high sensitivity, rapid response times, and the ability to detect multiple analytes simultaneously. Biosensors hold significant promise for revolutionizing pesticide residue analysis by enabling real-time, on-site detection and analysis. This advancement could significantly improve food safety monitoring and regulatory compliance efforts.

7. Conclusions

The pesticide residues analysis in food is essential for ensuring food safety and protecting human health. Analytical techniques play a crucial role in detecting and quantifying pesticide residues in various food products. These techniques, along with sample extraction and cleanup techniques, enable the accurate and reliable analysis of pesticide residues, helping to ensure that food products are within acceptable limits and safe for consumption.

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