

Neonicotinoid residues in fruits, vegetables, and honey: advances in ultra-trace analysis, matrix-effect mitigation, and environmental risk monitoring

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Neonicotinoid residues in fruits, vegetables, and honey: advances in ultra-trace analysis, matrix-effect mitigation, and environmental risk monitoring

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Abstract

Neonicotinoid insecticides are widely used worldwide and have become emerging contaminants of concern due to their persistence, mobility, non-target ecological effects, and potential risks associated with chronic dietary exposure. Residues detected in fruits, vegetables, and honey represent important indicators of agricultural contamination pathways, environmental transport, and human exposure risks. This review critically evaluates recent advances from 2019 to 2026 in neonicotinoid residue monitoring, focusing on analytical innovations, matrix-related challenges, regulatory limitations, and future hazard surveillance strategies. Complex food matrices, particularly sugar-rich honey and pigment-rich vegetables, remain critical barriers because co-extracted compounds can compromise residue quantification and risk assessment. Advances in extraction optimization, calibration strategies, and advanced mass spectrometric techniques have improved detection reliability and exposure evaluation. Rapid sensing technologies provide opportunities for large-scale screening but require validation against established laboratory methods. Future monitoring frameworks should integrate predictive modelling, digital surveillance, and harmonized regulatory approaches to improve contaminant tracking and risk-based decision-making. Such integration is essential for protecting human health, preserving pollinator ecosystems, and strengthening sustainable food safety management.

Keywords: Analytical harmonization; food safety governance; maximum residue limits; neonicotinoid residues; pollinator-sensitive food systems; risk-based surveillance

1. Introduction

neonicotinoid insecticides (NEOs) occupy a contested position in contemporary food systems. On the one hand, they have been widely adopted because they provide effective crop protection against sap-sucking and chewing pests, support yield stability, and offer systemic activity through seed treatments, soil applications, and foliar sprays. Since their commercialization in the early 1990s, NEOs have been promoted as alternatives to

organophosphates and carbamates because of their selective action on insect nicotinic acetylcholine receptors (nAChRs) and comparatively lower acute toxicity in mammals (Barton et al. 2024). Their systemic uptake, broad-spectrum efficacy, and compatibility with modern crop-protection practices have contributed to extensive use across cereal, oilseed, fruit, and vegetable production systems (Kazimierczak et al. 2022; Woodcock et al. 2017). Their systemic activity, high oral potency to insects, and convenient seed- and foliar-treatment formulations have further accelerated adoption across global cropping systems (Yang et al. 2026). On the other hand, this agronomic utility creates a food-security tension because repeated and high-frequency application can increase environmental persistence, non-target organism exposure, dietary residue concerns, and regulatory scrutiny (Cui et al. 2024).

This tension is particularly important because food security is not limited to food availability; it also depends on food safety, ecological sustainability, consumer protection, and the reliability of governance systems that regulate agricultural inputs. NEOs can enter food matrices through several pathways. As systemic compounds, they are absorbed by plant tissues after seed treatment, soil drench, or foliar application and may remain as residues in edible tissues such as fruit flesh, peels, leaves, nectar, and pollen. Runoff, spray drift, and environmental transport may also distribute residues into adjacent crops, apiaries, and surrounding ecosystems, while some metabolites may remain biologically active or persist longer than parent compounds (Li et al. 2024). These properties explain the recurrent detection of NEO residues in fruits, vegetables, and honey and justify their inclusion in routine residue-monitoring programs. The major commercial NEO differ in molecular structure, water solubility, polarity, and octanol–water partitioning, which influence their environmental mobility, residue persistence, extraction behavior, and analytical detectability in food matrices (Table 1). The challenges associated with neonicotinoid residues are directly connected to the United Nations Sustainable Development Goals (SDGs), particularly SDG 2 (Zero Hunger), which emphasizes sustainable food production and resilient agricultural systems; SDG 3 (Good Health and Well-being), through the protection of consumers from chemical exposure; and SDG 12 (Responsible Consumption and Production), which promotes safer and more sustainable management of agricultural inputs. Therefore, effective residue monitoring represents an important component of achieving sustainable food systems while balancing agricultural productivity, environmental protection, and public health.

The toxicological and ecological implications of NEO residues remain complex. Reported acute oral LD₅₀ values in mammals are typically in the range of 150–500 mg/kg body weight for imidacloprid and clothianidin, whereas chronic NOAEL values derived from rodent studies range between approximately 5–10 mg/kg bw/day, depending on the compound and endpoint evaluated (Alkharashi et al. 2026). Regulatory toxicological benchmarks established by authorities such as the European Food Safety Authority and the United States Environmental Protection Agency define acceptable daily intake (ADI) values generally in the range of 0.02–0.06 mg/kg bw/day and acute reference doses (ARfD) of similar magnitude (Katić et al. 2021). Dietary exposure assessments usually estimate chronic intake using supervised residue trial median values and food-consumption data, while acute exposure models apply highest residue levels. Risk characterization is then performed using hazard quotients, where hazard quotient (HQ) < 1 indicates acceptable risk under the assumptions applied (Ambrus et al. 2023). Although national and regional surveillance programs often report dietary exposure levels below established toxicological reference values, unresolved uncertainties remain concerning chronic low-dose exposure, metabolite toxicity, cumulative and mixture effects, and vulnerable groups such as infants and pregnant women (Antonangeli et al. 2023; ZhangLu 2022). Recent biomonitoring and epidemiological studies have suggested associations between urinary NEO metabolites and neurodevelopmental or metabolic endpoints,

although causal interpretation remains limited by co-exposure, confounding variables, and insufficient longitudinal evidence (Nishihama et al. 2023). Therefore, integrating mechanistic toxicology with probabilistic exposure modelling remains necessary for refining cumulative and mixture risk assessment in food systems (D'Amore 2026).

Beyond human dietary exposure, NEOs have generated major concern because of their potential effects on pollinators and ecological communities. Laboratory, semi-field, and field studies have linked NEO exposure to acute mortality and sublethal effects in bees and other pollinators, including impaired foraging, navigation, learning, colony growth, and pathogen resistance. These effects may interact with habitat loss, pathogens, climate stressors, and other agrochemicals, thereby contributing to broader declines in pollinator abundance and diversity (Chreil et al. 2024). As a result, pollinator safety has become a central criterion in NEO risk assessment and policy decision-making (Mota et al. 2024). In addition, extensive use of neonicotinoid insecticides has contributed to the evolution of resistance in several important pest taxa, including aphids, whiteflies, and planthoppers. Resistance mechanisms involve both target-site alterations of nicotinic acetylcholine receptors (nAChRs) and enhanced metabolic detoxification, particularly through cytochrome P450 monooxygenases. These mechanisms can reduce field efficacy, promote increased application rates or chemical replacement, and create challenges for integrated pest management (IPM) and long-term crop-protection sustainability (Nauen et al. 2022).

A second major challenge concerns governance. Regulatory responses to NEOs differ substantially across jurisdictions. The European Union has restricted outdoor uses of several active substances, including imidacloprid, clothianidin, and thiamethoxam, primarily because of pollinator-risk concerns, whereas other regions, including the United States and Canada, have adopted mitigation measures, conditional registrations, or time-limited emergency authorizations. Legal decisions in the European Union concerning emergency derogations under Regulation (EC) No 1107/2009 have also influenced national authorization practices and clarified the conditions under which seed-applied uses may be granted (Dentzman et al. 2025; Yang et al. 2025). This regulatory divergence affects approval status, treated-seed use, residue definitions, and re-evaluation schedules. It also creates practical challenges for international trade because maximum residue limits (MRLs), default limits, and analytical enforcement capacities vary across regulatory systems.

MRLs function as critical governance instruments because they translate toxicological evaluation, good agricultural practice, and analytical feasibility into enforceable food-safety standards. However, divergence between Codex standards, European Union MRLs, and national residue limits may create trade disparities, especially when an active substance is restricted in one jurisdiction but remains authorized elsewhere. Recent European monitoring reports show that official residue-control programs continue to use MRL exceedance, non-compliance, and residue occurrence data as core indicators for food-safety enforcement and risk-based surveillance (European Food Safety et al. 2026). These differences demonstrate that residue monitoring is not merely a laboratory activity; it is part of global food safety governance, affecting consumer protection, market access, and confidence in cross-border food supply chains. Reliable governance depends on reliable data. For NEO residues, analytical reliability is difficult because fruits, vegetables, and honey contain complex matrix constituents such as sugars, organic acids, pigments, lipids, waxes, and pollen-derived compounds. These constituents can interfere with extraction efficiency, chromatographic separation, and electrospray ionization, producing matrix effects that compromise quantification at low $\mu\text{g/kg}$ or sub- $\mu\text{g/kg}$ levels. Effective monitoring therefore requires validated, matrix-specific, and comparable analytical workflows. Method validation must

address limit of quantification, recovery, precision, selectivity, linearity, matrix effects, measurement uncertainty, and analyte stability. Reliable risk management requires validated analytical methods, harmonized performance criteria, and integration of international MRL regulations into exposure-assessment workflows (FerrariSpeltini 2023). Contemporary reviews also emphasize the importance of harmonized validation criteria and advanced LC–MS/MS or high-resolution mass spectrometry (HRMS)-based methods to ensure accurate quantification at increasingly stringent regulatory thresholds (Hernández-MesaMoreno-González 2022).

Analytical advances since 2019 have improved the detection, quantification, and multi-residue profiling of NEOs in food matrices. Modified quick, easy, cheap, effective, rugged, and safe extraction (QuEChERS) extraction protocols combined with dispersive solid-phase extraction (d-SPE) have improved recoveries and reduced matrix effects, particularly in sugar-rich and pigment-rich commodities (Shin et al. 2022). Ultra-high performance liquid chromatography coupled to tandem mass spectrometry (UHPLC–MS/MS) methods now routinely achieve low $\mu\text{g/kg}$ to sub- $\mu\text{g/kg}$ limits of quantification in compliance with international regulatory requirements (Yang et al. 2023). High-resolution mass spectrometry, including Orbitrap and quadrupole time-of-flight (QToF) platforms, further improves selectivity, mass accuracy, retrospective screening, and metabolite identification. These developments enable more refined dietary exposure assessments, source attribution, and regulatory confirmation. Nevertheless, inter-laboratory differences in extraction, cleanup, calibration, matrix-effect correction, and mass transitions continue to limit comparability across surveillance systems (Tang et al. 2025). Therefore, the analytical problem is inseparable from the governance problem: without harmonized and matrix-appropriate methods, residue datasets cannot reliably support exposure assessment, MRL enforcement, trade decisions, or food-safety policy. Figure 1 summarizes the overall pathways of NEO contamination, exposure routes, environmental distribution, and current monitoring strategies discussed in this review.

Existing reviews have provided valuable syntheses of NEO toxicology, environmental fate, sample preparation, chromatographic detection, and rapid screening technologies (FerrariSpeltini 2023; Wang et al. 2022). Integrated analytical studies have also demonstrated the value of combining parent compounds and transformation products in food matrices to strengthen monitoring relevance (Calza et al. 2022). However, many reviews remain method-centered and do not sufficiently integrate analytical reliability with regulatory harmonization, food-safety surveillance, international trade, vulnerable-population protection, and food-security governance. This gap is important because the effectiveness of residue monitoring depends not only on instrument sensitivity, but also on whether monitoring data are comparable, interpretable, and usable for policy decisions across diverse food systems and regulatory contexts.

Accordingly, this review evaluates recent advances from 2019 to 2026 in NEO residue monitoring in fruits, vegetables, and honey as tools for global food safety governance. Specifically, it examines the capabilities and limitations of UHPLC–MS/MS and HRMS for ultra-trace detection in complex food matrices, assesses how modern sample-preparation strategies improve extraction efficiency and reduce matrix effects, analyzes the role of validation criteria and regulatory frameworks in strengthening monitoring reliability, and evaluates rapid and portable detection technologies as complementary tools for risk-based surveillance. By linking analytical innovation with regulatory harmonization and food-security implications, this review provides a matrix-oriented and governance-relevant synthesis to support accurate exposure assessment, international monitoring comparability, and more resilient food safety systems.

2. Methodology

This review used a systematic literature search to examine recent studies on NEO residue monitoring in fruits, vegetables, and honey. The search was conducted on March 2026 and covered studies published from 2019 to 2026. Articles were collected from Scopus, Web of Science, ScienceDirect, and PubMed using the Boolean search string: (“NEO” OR imidacloprid OR clothianidin OR thiamethoxam OR acetamiprid OR dinotefuran OR nitenpyram) AND (“residue” OR “pesticide residue*” OR MRL OR “dietary exposure” OR monitoring) AND (“fruit*” OR “vegetable*” OR honey OR food) AND (“LC-MS/MS” OR “UHPLC-MS/MS” OR HRMS OR QuEChERS OR “matrix effect*” OR immunoassay OR electrochemical OR SERS OR microfluidic)**. Relevant policy and regulatory documents from EFSA, FAO/WHO JMPR, Codex Alimentarius, and EU SANTE/EURL were also included to support the discussion on residue limits, monitoring standards, and food safety governance. Wikipedia, non-authoritative websites, studies outside the selected date range, papers unrelated to food matrices, and studies without clear analytical or regulatory relevance were excluded.

3. Risk Assessment, Quality Assurance, and Regulatory Perspectives in NEO Monitoring

NEO residue monitoring should be understood not only as a technical activity, but also as a core component of food safety governance infrastructure. In global food systems, residue data connect agricultural pesticide use with dietary exposure assessment, regulatory enforcement, trade compliance, and consumer protection. NEOs continue to be among the most widely used systemic insecticides worldwide. Their persistence, water solubility, and broad-spectrum activity have led to frequent detection in fruits, vegetables, and honey, thereby triggering regulatory attention and intensive monitoring programs. Effective risk management depends on three interconnected elements: (1) robust analytical method validation and laboratory quality assurance; (2) coherent performance criteria and surveillance design; and (3) integration of international and regional MRL frameworks into exposure and decision-making workflows (Kueh-Tai et al. 2025). At the analytical level, method validation and laboratory quality control are prerequisites for generating defensible residue data. Current EU/SANTE guidance (SANTE/11312/2021) and EURL documents specify performance criteria including limit of quantification (LOQ), trueness or recovery, precision, repeatability and reproducibility, linearity, selectivity, matrix effects, measurement uncertainty, and analyte stability. Acceptance criteria generally require mean recoveries of 70–120%, relative standard deviations $\leq 20\%$, and LOQs at or below applicable MRLs (Kuzniarová et al. 2025). The use of matrix-matched calibration and isotopically labelled internal standards is particularly important for compensating ion suppression or enhancement in complex matrices such as honey and leafy vegetables. Participation in proficiency testing further strengthens inter-laboratory comparability. These quality assurance measures directly influence the reliability of surveillance datasets used in exposure assessment (Pacini et al. 2025).

Residue monitoring data generated under validated conditions provide the empirical basis for dietary risk assessment. Estimated daily intake (EDI) values are calculated by combining measured residue concentrations with food consumption data and are then compared with toxicological reference values such as the ADI and ARfD established by bodies including the Codex Alimentarius and national authorities. When metabolites are included in the residue definition, high-resolution mass spectrometry data may also support cumulative exposure evaluation. However, uncertainty in analytical quantification, particularly near LOQ or MRL thresholds, can significantly influence risk characterization outcomes (Stehle et al. 2023). This point is critical for food safety governance because a small analytical deviation may affect whether a food product is classified as compliant, non-compliant, or requiring further investigation.

Regulatory frameworks translate risk assessment results into enforceable standards. MRLs are established by international bodies such as the Codex Alimentarius, based on JMPR evaluations, and by regional authorities under legislative instruments such as Regulation (EC) No 396/2005. These limits serve multiple governance functions: they protect consumers, guide agricultural practice, support official control programs, and provide benchmarks for domestic and international trade. However, divergence between Codex and regional MRLs may result in trade disparities, especially when substances are restricted or approvals are withdrawn in one jurisdiction while remaining authorized in another. In such cases, default LOQs, such as 0.01 mg/kg in the EU, may become enforcement thresholds. Consequently, regulatory decision-making depends not only on toxicological benchmarks but also on analytical feasibility, method performance characteristics, and measurement uncertainty budgets (Zhang et al. 2024). For global food security, this regulatory variation has practical implications. Countries with strong analytical infrastructure may enforce low MRLs, include metabolites in monitoring programs, and apply confirmatory LC–MS/MS or HRMS methods. In contrast, countries with limited laboratory capacity may rely on narrower residue panels, less frequent surveillance, or non-harmonized methods. This imbalance can affect market access, consumer confidence, and the comparability of food safety data across regions. Therefore, strengthening NEO monitoring requires not only better detection technology, but also harmonized validation criteria, transparent residue definitions, inter-laboratory comparability, and risk-based surveillance strategies. Overall, NEO residue monitoring functions as a bridge between analytical chemistry and food-system governance. Reliable methods produce comparable data; comparable data support exposure assessment; exposure assessment informs regulatory enforcement; and regulatory enforcement contributes to trade compliance, consumer protection, and sustainable food-system governance. This framework is particularly important for fruits, vegetables, and honey because these commodities differ in matrix complexity, consumption patterns, trade relevance, and potential ecological links to pollinator exposure. Representative MRLs for selected NEOs are summarized in Table 2.

4. Advances in Sample Preparation Strategies for Complex Food Matrices

Reliable NEO residue monitoring in fruits, vegetables, and honey depends strongly on sample preparation because each matrix presents different analytical interferences. Sample preparation is therefore not only a laboratory step, but also a determinant of data reliability, regulatory confidence, and comparability across surveillance programs. Between 2019 and 2026, classical approaches such as QuEChERS and dispersive solid-phase extraction were refined, while miniaturized and solvent-saving extraction methods were increasingly explored to improve residue detection in high-water and high-sugar matrices (Berenguer et al. 2023). Fruits and vegetables generally contain high levels of water, sugars, organic acids, pigments, waxes, and plant-derived compounds. These components can reduce extraction efficiency, increase matrix effects, and affect quantification when residue levels are close to regulatory limits. For many fruit and vegetable matrices, QuEChERS remains the main sample preparation approach because it offers practical extraction, acceptable recovery, and compatibility with LC–MS/MS-based multiresidue analysis. Recent developments have focused on improving recovery, reducing co-extracted interferences, and maintaining method performance across commodities with different water, pigment, and organic-acid contents (Câmara et al. 2022; Melo et al. 2020). Comparative studies have shown that optimized QuEChERS workflows can provide more consistent recoveries than conventional liquid–liquid extraction for many pesticide residues, supporting their use in routine monitoring program (Shin et al. 2022).

However, fruits and vegetables should not be treated as a single analytical category. High-water matrices such as tomato and lettuce are generally more compatible with standard QuEChERS-based workflows, whereas

pigment-rich leafy vegetables often require more careful cleanup because chlorophyll and other plant compounds can intensify ion suppression. This distinction is important for regulatory monitoring because insufficient matrix cleanup can produce unreliable residue estimates, especially when results are near the LOQ or MRL threshold. In such cases, matrix-matched calibration, appropriate cleanup, and internal-standard correction are necessary to reduce false compliance or false exceedance risks. Honey represents a more difficult analytical matrix than most fruits and vegetables because of its high sugar content, viscosity, and possible presence of pollen, waxes, pigments, and bee-derived materials. These components can interfere with extraction, clog analytical systems, and suppress ionization during LC–MS/MS analysis. For this reason, honey usually requires matrix-specific adaptation rather than direct transfer of fruit or vegetable protocols. Validated studies have used modified QuEChERS, dilution-assisted extraction, dispersive SPE, freezing-out, or related cleanup strategies to reduce sugar co-extraction and achieve low LOQs with acceptable recovery (Lasheras et al. 2021). These adaptations are essential because honey is both a food commodity and an indirect indicator of pesticide exposure in agroecosystems and apiary environments.

d-SPE and related cleanup strategies remain important because they reduce matrix-derived interferences before instrumental analysis. Instead of selecting cleanup materials only for chemical convenience, monitoring laboratories must match cleanup intensity to matrix risk. Fruits with waxes and pigments, leafy vegetables with chlorophyll-rich extracts, and honey with carbohydrate-rich residues require different cleanup priorities. Recent studies show that tailored cleanup can improve signal quality and reduce analytical uncertainty without excessive analyte loss (Lewiński et al. 2023). This supports more defensible residue data for exposure assessment and regulatory enforcement. Miniaturized extraction and microextraction approaches have expanded the available options for trace-level monitoring. These methods can reduce solvent use, improve enrichment, and support lower detection limits, especially when residues occur at ultra-trace levels (NotardonatoAvino 2024; Zareiyan et al. 2024). Solid-phase microextraction (SPME) and related low-solvent approaches may also support rapid or field-oriented screening when combined with appropriate validation and confirmatory analysis (Díaz et al. 2023; Souza et al. 2021).

Across the three commodity groups, the main methodological lesson is that sample preparation must be matrix-adapted rather than universally applied. Fruits usually require control of sugars, acids, pigments, and waxes; vegetables, especially leafy vegetables, require stronger attention to pigment-related ion suppression; and honey requires specific strategies to manage sugar load, viscosity, and bee-derived co-extractives. Hybrid workflows that combine bulk extraction, cleanup, and enrichment can improve sensitivity when ultra-trace monitoring is required, but they must remain practical for surveillance laboratories (Quang Trung et al. 2025). Automation and 96-well plate adaptations may further improve throughput and reduce labor costs, provided that validation demonstrates acceptable recovery, matrix-effect control, and measurement uncertainty (Berenguer et al. 2023; Melo et al. 2020). Table 3 summarizes representative analytical method parameters for NEO residue determination in fruits, vegetables, and honey, emphasizing how sample preparation, detection platform, LOQ, recovery, throughput, and regulatory suitability jointly determine monitoring reliability.

5. High-Resolution Chromatographic Techniques for Multi-Residue NEO Analysis

NEO residues present analytical challenges because parent compounds and metabolites differ in polarity, stability, and retention behavior, while fruits, leafy vegetables, and honey contain diverse matrix interferences. For food safety governance, chromatographic techniques are important not only because they separate analytes,

but because they determine whether residue data can reliably support MRL enforcement, dietary exposure assessment, and cross-laboratory comparability. Modern monitoring therefore requires chromatographic systems that provide adequate sensitivity, selectivity, and reproducibility across matrix types (Visconti Gioele et al. 2024). UHPLC–MS/MS remains the main platform for routine NEO residue monitoring because it combines short analysis time, high sensitivity, and strong confirmatory capability. When paired with suitable sample preparation, UHPLC–MS/MS can achieve low $\mu\text{g/kg}$ LOQs across fruits, vegetables, and honey, making it suitable for compliance testing under increasingly strict regulatory limits. Recent applications have demonstrated reliable quantification of imidacloprid, acetamiprid, clothianidin, thiamethoxam, and related metabolites in vegetable and honey matrices (Yang et al. 2023). However, matrix-matched calibration and isotope-labelled internal standards remain essential because co-extracted sugars, pigments, and organic acids may affect ionization and compromise regulatory interpretation near MRL thresholds (Ahn et al. 2022).

Complementary chromatographic strategies such as hydrophilic interaction liquid chromatography (HILIC), mixed-mode separation, and multidimensional liquid chromatography (LC) are useful when routine reversed-phase workflows cannot adequately retain highly polar NEO metabolites or separate co-eluting matrix interferences. Their main value is not methodological novelty, but improved monitoring confidence when residue definitions include polar metabolites or when complex matrices such as honey and pollen require stronger separation capacity (PapatheocharidouSamanidou 2023; Valverde et al. 2022). Two-dimensional LC approaches may also improve method coverage by combining separation mechanisms for polar and less-polar analytes, thereby reducing false positives and false negatives in surveillance datasets (JostHabedank 2020). Nevertheless, these approaches require greater instrumental capacity, method development expertise, and data handling; therefore, they are better positioned for confirmatory laboratories or targeted surveillance rather than routine large-scale monitoring. Gas chromatography (GC) methods have a more limited role in NEO residue analysis because many NEOs are polar or thermolabile. Although derivatization or chemical conversion can make selected compounds compatible with GC-MS workflows, this adds sample-handling complexity and may introduce transformation-related uncertainty. Consequently, GC-based approaches are most relevant for laboratories already operating legacy pesticide workflows or for selected compound groups where complementary selectivity is required (Wahab et al. 2022; Zeng et al. 2024).

Overall, chromatographic method selection should be driven by surveillance purpose rather than analytical sophistication alone. Routine enforcement programs require robust UHPLC–MS/MS methods with validated LOQs, recovery, and matrix-effect control. Targeted investigations and metabolite-inclusive monitoring may require HILIC, mixed-mode, HRMS-compatible workflows, or multidimensional LC. For global food safety governance, the key requirement is that chromatographic methods generate comparable, defensible, and policy-relevant residue data across commodities and jurisdictions. In this context, advanced chromatographic techniques strengthen food-system surveillance only when they improve regulatory confidence, reduce uncertainty near MRL thresholds, and support harmonized interpretation of NEO residue occurrence in fruits, vegetables, and honey (Visconti Gioele et al. 2024)

6. Mass Spectrometry Innovations for Ultra-Trace Detection and Structural Confirmation

UHPLC–MS/MS and HRMS play complementary roles in NEO residue monitoring. For routine enforcement, UHPLC–MS/MS remains the primary platform because it provides high sensitivity, strong selectivity, relatively standardized workflows, and validated quantification at low $\mu\text{g/kg}$ levels. These characteristics make it suitable

for official control programs that require consistent comparison of residue levels with maximum residue limits across large numbers of fruit, vegetable, and honey samples. HRMS has a different but increasingly important function in food safety surveillance. Instruments such as Orbitrap and QToF systems support accurate-mass measurement, improved structural confirmation, and broader screening of known and suspected residues in complex food matrices (Sun et al. 2023). Compared with routine UHPLC–MS/MS workflows, HRMS is particularly valuable when monitoring programs need to confirm uncertain findings, investigate metabolites or transformation products, or respond to changing regulatory residue definitions. Recent method papers and reviews emphasize that platform selection should be guided by surveillance purpose, namely routine quantification, confirmatory analysis, or suspect screening, rather than by instrument sophistication alone (Hernández-MesaMoreno-González 2022; Saito-Shida et al. 2021).

For confirmatory analysis, HRMS strengthens regulatory confidence by combining retention-time information, accurate mass, isotope-pattern evaluation, and product-ion evidence. These criteria help distinguish NEO residues from matrix interferences in sugar-rich honey, pigment-rich vegetables, and chemically complex fruit extracts. Targeted HRMS workflows can quantify residues while also preserving full-scan data for later re-examination. Suspect and non-target workflows further allow laboratories to search for unexpected metabolites, degradates, or unauthorized substances without re-analyzing stored samples (Wang et al. 2025; Zianni et al. 2023). Data-dependent acquisition and data-independent acquisition (DIA) provide additional fragmentation information for compound confirmation, although DIA requires careful data interpretation when co-eluting compounds are present (Kavanagh et al. 2021). The main governance value of HRMS is retrospective surveillance. As maximum residue limits, residue definitions, and priority pesticide lists change, archived HRMS datasets can be reprocessed to check for newly regulated compounds or metabolites. This capacity is especially useful for food safety agencies facing evolving NEO regulations and limited resources for repeated sampling. Practical applications have shown that HRMS-based workflows can confirm low- $\mu\text{g}/\text{kg}$ NEO residues in honey and other food matrices, while also supporting metabolite-inclusive monitoring relevant to exposure assessment and regulatory decision-making (Almeida et al. 2025).

7. Rapid and Portable Detection Technologies for On-Site Screening

Rapid and portable detection technologies can strengthen decentralized monitoring capacity for NEO residues, particularly in settings where access to advanced laboratory infrastructure is limited. Their main contribution is not to replace confirmatory laboratory analysis, but to support early screening, border inspection, market surveillance, on-farm checks, and risk-based sample prioritization. In food safety systems, these tools can reduce the number of unnecessary laboratory submissions, accelerate decision-making, and help monitoring agencies identify samples that require confirmatory LC–MS/MS or HRMS analysis (Barton et al. 2024; Han et al. 2025). Recent studies have reported field-oriented platforms based on immunoassays, electrochemical biosensors, surface-enhanced Raman spectroscopy (SERS), microfluidic devices, paper-based assays, and smartphone-assisted readouts for pesticide residue screening in fruits, vegetables, honey, pollen, and related matrices (Xu L. et al. 2022).

Immunoassay-based methods are among the most practical tools for first-line screening because they are relatively simple, rapid, and low-cost. LFIAs can provide visual or semi-quantitative results within minutes, making them useful for market inspection, border screening, and preliminary field triage. More advanced immunosensors can improve sensitivity and allow multiplexed detection, although their performance remains

affected by antibody cross-reactivity, matrix interference, and the need for sample dilution or cleanup in colored fruit extracts and honey (Xu M. et al. 2022). Therefore, immunoassays are best positioned as screening tools that identify suspect samples for confirmatory laboratory testing rather than as stand-alone enforcement methods. Recent developments in portable sensing platforms have enabled diverse rapid screening approaches for NEO residues across food and bee-related matrices. The analytical characteristics, detection performance, and field applicability of representative technologies are summarized in Table 4.

Electrochemical sensors also offer strong potential for decentralized monitoring because they are compact, relatively inexpensive, and compatible with portable readers. Screen-printed electrodes, aptamer-based sensors, molecularly imprinted polymers, and nanomaterial-modified electrodes have been developed for detecting imidacloprid, thiamethoxam, clothianidin, and related compounds (Nehru et al. 2024). Their advantages include direct electrical readout, low reagent consumption, and potential integration with smartphone-based systems (Almenhali et al. 2025; Haritha et al. 2023; Luo et al. 2022). However, food matrices can foul electrodes or introduce false signals, especially when extracts contain pigments, sugars, organic acids, or waxes. For this reason, electrochemical sensors require matrix-matched calibration, field quality control, and validation against LC–MS/MS before they can support regulatory escalation (Barton et al. 2024).

SERS-based platforms provide rapid molecular fingerprinting and can distinguish structurally related NEOs when substrate uniformity and spectral interpretation are well controlled (Abu Bakar et al. 2024). Their value for food-system surveillance lies in rapid screening of suspect samples with minimal reagent use. However, SERS performance can be affected by matrix fluorescence, uneven substrate response, and variable signal reproducibility, particularly in pigment-rich fruits and sugar-rich honey. These limitations mean that SERS should be used as a prioritization tool, not as the sole basis for regulatory enforcement (Xu L. et al. 2022). A clearer regulatory role will require standardized substrate production, matrix-specific validation, and comparison with confirmatory laboratory methods

Microfluidic and paper-based devices are especially relevant for low-resource settings because they can reduce reagent use, simplify sample handling, and support low-cost disposable testing. Lab-on-paper and chip-based formats can integrate extraction, cleanup, mixing, and detection into compact devices, making them suitable for decentralized screening in markets, border posts, and local monitoring stations (Rao et al. 2025; Zhang et al. 2021). Some microfluidic systems have also integrated electrochemical detection or SERS sampling to improve sensitivity and enable multiplexed pesticide screening (Cao et al. 2024). Their main limitation is the difficulty of incorporating robust cleanup for complex matrices such as viscous honey or pigment-rich fruit extracts.

Smartphone-linked readouts can strengthen decentralized surveillance when they are used for calibration, geotagging, data capture, and rapid reporting. Portable optical readers, miniaturized potentiostats, and smartphone cameras can support standardized recording of screening results and facilitate the mapping of residue-risk signals across markets, supply chains, apiaries, or border checkpoints. This function is useful for food safety governance because screening data can help agencies prioritize samples for confirmatory laboratory testing, identify high-risk commodities, and improve allocation of limited analytical resources (Luo et al. 2022; Sherard et al. 2023). However, smartphone-linked systems should not be treated as independent regulatory platforms unless their performance is validated against reference methods. Portable technologies should therefore be deployed within a tiered monitoring framework. In the first tier, rapid devices screen large numbers of samples and identify those with potential residue concerns. In the second tier, suspicious or policy-sensitive samples are submitted for

confirmatory LC-MS or HRMS. This approach is particularly useful for low-resource settings, import inspection, local market surveillance, and risk-based sampling because it expands monitoring reach without weakening regulatory confidence. Practical implementation requires matrix-matched validation, field quality-control samples, false positive and false negative assessment, clear decision thresholds, and confirmatory laboratory capacity (Calza et al. 2022; Kammoun et al. 2019; Xu L. et al. 2022). Artificial intelligence and Internet of Things (IoT) tools may support broader surveillance systems through data integration, geospatial mapping, and early-warning dashboards, but their role in NEO residue monitoring remains indirect. These systems can help organize field-screening results, identify spatial or temporal risk patterns, and guide targeted sampling; however, they do not directly verify residue concentrations. Therefore, their discussion should remain brief unless supported by residue-specific validation studies (Tatiya et al. 2025). As illustrated in Figure 2, recent advancements in rapid and portable detection technologies enable effective on-site screening of NEO residues across diverse sample matrices including fruits, vegetables, and honey. LFIA provides a simple visual readout for preliminary screening, whereas electrochemical sensors offer quantitative, real-time measurement. SERS allows highly specific molecular fingerprinting, and paper/microfluidic devices provide a low-cost, portable, and multiplex-capable platform suitable for field deployment. Collectively, these technologies facilitate rapid decision-making and prioritization of samples for confirmatory laboratory analysis.

8. Matrix Effects, Ion Suppression, and Analytical Challenges in Fruit, Vegetable, and Honey Systems

Matrix effects are a central source of uncertainty in NEO residue monitoring because they can alter the measured signal of target compounds in complex food extracts. In LC-MS/MS, co-extracted substances may suppress or enhance ionization, causing measured residue concentrations to appear lower or higher than their true values. This problem has direct regulatory implications. When residue levels are close to the LOQ or MRL, even moderate matrix effects can influence whether a sample is classified as compliant, non-compliant, or uncertain. Therefore, matrix effects are not only an analytical problem; they are also a food safety governance problem. The risk differs across commodities. Fruits may contain sugars, organic acids, pigments, and waxes that interfere with extraction and quantification. Leafy vegetables often contain chlorophyll, lipids, and cellular materials that can intensify signal suppression. Honey is particularly challenging because its high sugar content, viscosity, pollen, waxes, and pigment residues can interfere with extraction and instrumental detection. These differences mean that a method validated for one commodity cannot automatically be assumed reliable for another. Without matrix-specific validation, monitoring programs may produce false compliance, where unsafe or non-compliant residues are underestimated, or false exceedance, where compliant products are incorrectly classified as exceeding regulatory limits (BannoYabuki 2020; FerrariSpeltini 2023).

Matrix effects also affect cross-country comparability. International residue monitoring depends on the assumption that laboratories can generate comparable data for similar commodities. However, differences in sample preparation, cleanup, calibration, internal-standard use, and matrix-effect correction can produce divergent results across laboratories and jurisdictions. This is especially important for traded commodities such as fruits, vegetables, and honey, where a residue result may affect border inspection, market access, and consumer confidence. For this reason, matrix-matched calibration, isotopically labelled internal standards, recovery correction, measurement uncertainty estimation, and proficiency testing are essential for regulatory confidence, not merely for analytical optimization. Honey illustrates the governance relevance of matrix effects particularly well. Dilution alone may be insufficient when monitoring sub- $\mu\text{g/kg}$ residues because sugar-rich and pollen-

containing extracts can still suppress ionization or contaminate analytical systems. More robust workflows, including QuEChERS, solid-phase extraction (SPE), tailored cleanup, and internal-standard correction, are often required to obtain defensible quantification (Visconti Gioele et al. 2024). Similar logic applies to pigment-rich fruits and leafy vegetables, where insufficient cleanup may distort residue interpretation near regulatory thresholds. Overall, matrix effects should be treated as a determinant of monitoring reliability, regulatory confidence, and trade-relevant comparability. A governance-oriented monitoring system must require matrix-specific validation for major commodity groups, transparent reporting of recovery and uncertainty, and harmonized performance criteria across laboratories. Common matrix interferences and practical mitigation strategies are summarized in Table 5.

9. Future research Directions and emerging residue monitoring frameworks

Future research on NEO residue monitoring should move beyond improving detection sensitivity alone and toward developing intelligent, adaptive, and integrated surveillance systems. Although advances in UHPLC–MS/MS, HRMS, biosensors, and portable analytical platforms have substantially improved residue identification, current monitoring systems remain largely reactive. Conventional surveillance typically depends on periodic sampling followed by laboratory confirmation, which limits the ability to predict emerging contamination patterns, identify high-risk production areas, and rapidly respond to food safety threats. Future monitoring strategies should therefore incorporate artificial intelligence (AI), machine learning (ML), Internet of Things (IoT), and digital food-system technologies to transform residue monitoring from a laboratory-centered activity into a predictive and risk-based governance framework. AI-assisted surveillance could integrate analytical results, agricultural practices, climate variables, geographic information, and supply-chain data to generate dynamic predictions of residue occurrence and exposure risks (D’Amore 2026).

One promising research direction is the development of AI-driven predictive models for forecasting NEO residue contamination before extensive sampling is conducted. Machine learning algorithms, including random forests, gradient boosting models, support vector machines, and deep neural networks, can analyze complex relationships between pesticide application patterns, crop characteristics, environmental conditions, and historical residue datasets. These models may identify hidden risk factors that are difficult to detect through conventional statistical approaches. For example, residue accumulation may depend not only on application frequency but also on temperature, rainfall, soil properties, irrigation practices, crop growth stage, and surrounding ecological conditions. Integrating these variables into predictive models could support risk-based sampling strategies, where regulatory agencies prioritize commodities, locations, and seasons with the highest probability of residue exceedance. However, future studies must address model transparency, validation across geographical regions, and uncertainty quantification because inaccurate or poorly generalized AI predictions may introduce new regulatory biases (Li et al. 2024). Another important research pathway involves the integration of AI with advanced analytical instrumentation. Modern HRMS platforms generate large-scale datasets containing thousands of molecular features, including parent compounds, metabolites, transformation products, and unknown chemical signals. Manual interpretation of these datasets remains challenging because it requires extensive expert knowledge and time-consuming data processing. AI-based approaches, particularly deep learning and automated spectral interpretation systems, have potential to accelerate compound identification, suspect screening, and retrospective analysis. Future research should focus on developing standardized AI-assisted workflows that can recognize NEO-related molecular patterns, prioritize suspicious signals, and improve metabolite identification

accuracy. Such systems would be particularly valuable because regulatory definitions of pesticide residues increasingly consider transformation products and cumulative exposure rather than only parent compounds (Hernández-MesaMoreno-González 2022; Wang et al. 2025).

The combination of AI with portable detection technologies represents another major opportunity for decentralized residue monitoring. Current rapid detection platforms, including electrochemical sensors, SERS, immunoassays, and microfluidic devices, provide rapid screening capabilities but often require sophisticated interpretation and calibration. AI-enhanced sensor systems could improve signal recognition, compensate for matrix interference, and enable real-time decision-making through smartphone-based applications. For example, machine learning algorithms could analyze spectral fingerprints from SERS platforms or electrochemical response patterns to distinguish NEO residues from interfering compounds in complex matrices such as honey, leafy vegetables, and fruits. Future research should prioritize the development of validated AI-sensor combinations that maintain analytical reliability under field conditions rather than only demonstrating performance under controlled laboratory environments (Abu Bakar et al. 2024; Almenhali et al. 2025). A critical research priority is the establishment of internationally harmonized datasets for AI development. Machine learning performance depends strongly on the quality, diversity, and representativeness of training data. Currently, NEO residue datasets vary substantially in analytical methods, reporting formats, commodities examined, geographic coverage, and residue definitions. These inconsistencies limit model transferability across countries and regulatory systems. Future collaborative research should establish standardized open-access databases containing validated residue concentrations, analytical uncertainty information, sample metadata, agricultural practices, and environmental parameters. Such databases would improve reproducibility, reduce algorithmic bias, and support global cooperation in food safety monitoring. International harmonization should therefore become a parallel objective alongside technological innovation (FerrariSpeltini 2023; Pacini et al. 2025).

10. Conclusions

NEO residues represent a continuing challenge at the interface of chemical hazard management, food safety, and ecosystem protection. This review demonstrates that effective surveillance of neonicotinoids in fruits, vegetables, and honey requires a transition from conventional residue determination toward integrated, risk-based monitoring frameworks that combine analytical robustness, regulatory harmonization, and predictive capabilities. Although significant advances have been achieved through modified QuEChERS extraction, matrix-specific cleanup strategies, UHPLC–MS/MS quantification, and HRMS-based structural confirmation, analytical uncertainty associated with complex food matrices remains a critical limitation for reliable exposure assessment and regulatory decision-making. The evidence indicates that residue monitoring cannot rely solely on increased detection sensitivity; rather, analytical performance must be accompanied by standardized validation criteria, transparent uncertainty evaluation, metabolite-inclusive residue definitions, and improved inter-laboratory comparability. Rapid sensing technologies, including biosensors, SERS, and microfluidic platforms, provide valuable opportunities for decentralized screening and early risk identification, but their application should remain integrated within tiered surveillance systems supported by confirmatory laboratory analysis.

Future progress in neonicotinoid hazard management will depend on the convergence of advanced analytical chemistry with digital technologies, including artificial intelligence, machine learning, and environmental data integration. Such approaches may enable predictive identification of contamination hotspots, optimize sampling strategies, and strengthen early-warning systems. However, technological innovation must be accompanied by

internationally coordinated datasets, harmonized regulatory frameworks, and capacity development to ensure equitable implementation across regions. Overall, safeguarding food systems from neonicotinoid-related hazards requires a holistic strategy that links molecular-level detection with population exposure assessment, ecological risk considerations, and sustainable agricultural governance. By integrating high-confidence analytical methods, predictive surveillance, and globally coordinated risk management, future monitoring systems can provide stronger protection for consumers, pollinators, and the long-term resilience of agroecosystems.

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Credit authorship contribution statement

Steven Suryoprabowo: Investigation. Writing – original draft. **Zhongxing Wang:** Visualization. **Wenbin Wang:** Supervision, Investigation. **Yahui Guo:** writing-review & editing. **Dody Andi Winarto:** Conceptualization, Investigation. **Nur Sri Wahyuni:** writing-review & editing, Investigation. **Eddy Seong Guan Cheah:** Investigation, Supervision. **Elya Mufidah:** Investigation. **Retno Tri Astuti:** Conceptualization.

Declaration of competing interests

The authors declare that they are no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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Data sharing statement

No new data generated or analyzed.

Captions:

Figure 1. Integrated framework for neonicotinoid residue monitoring in complex food matrices.

Figure 2. Emerging rapid and portable technologies for decentralized NEO residue surveillance.

Table 1. Physicochemical determinants governing neonicotinoid environmental behavior and analytical detectability.

Table 2. Regulatory variability of MRLs in mg/Kg for selected NEO across food commodities and jurisdictions.

Table 3. Performance comparison of analytical workflows for NEO residue determination in food matrices.

Table 4. Characteristics and application potential of rapid screening technologies for NEO monitoring.

Table 5. Matrix-driven analytical challenges and mitigation strategies for LC–MS-based NEO residue analysis.

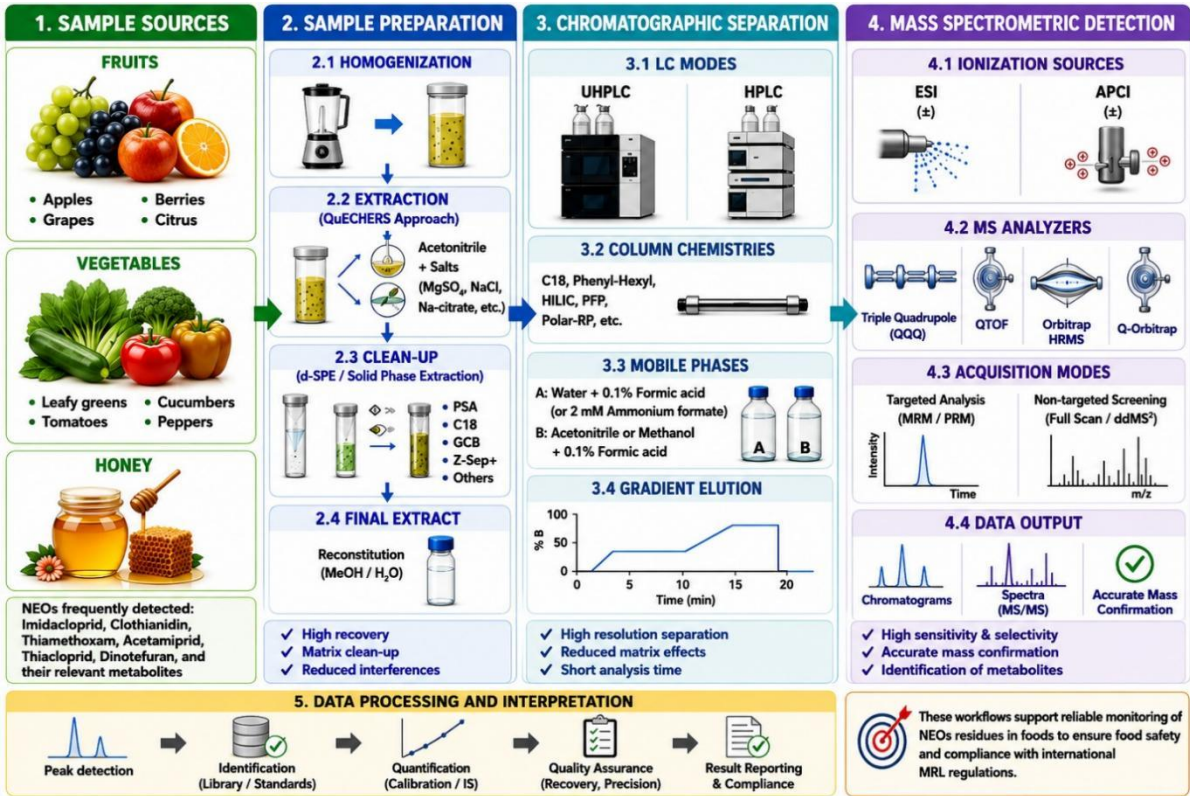


Figure 1. Integrated framework for NEO residue monitoring in complex food matrices.

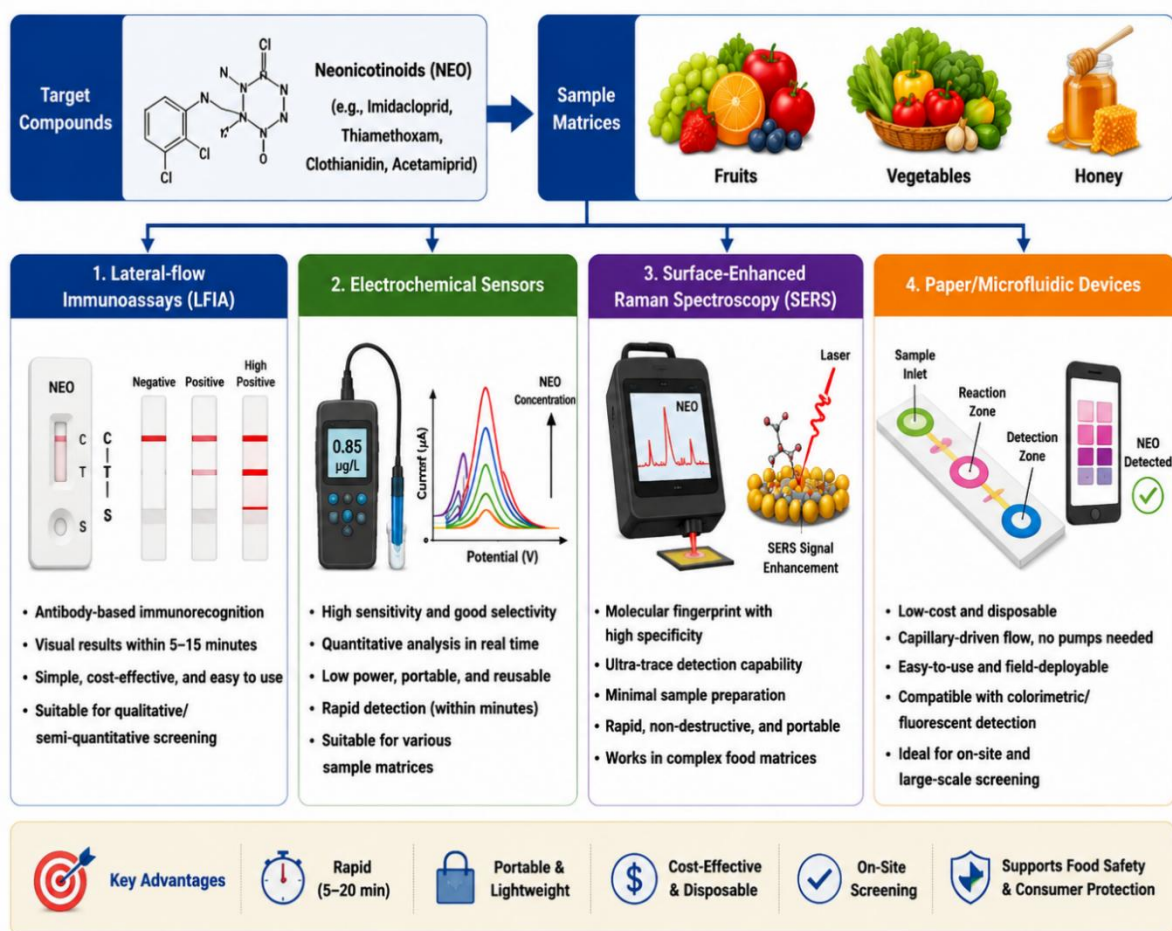
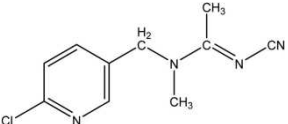
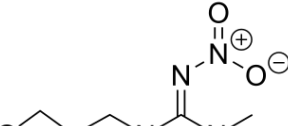
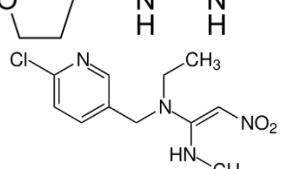


Figure 2. Emerging rapid and portable technologies for decentralized NEO residue surveillance.

Table 1. Physicochemical determinants governing NEO environmental behavior and analytical detectability (Pietrzak et al. 2020) (ZhangJiang 2025).

Compound	Structure	Molecular formula	Molecular weight (g/mol)	Water solubility* (mg/L - 20°C, pH=7)	Log K _{ow} (octanol-water)
Imidacloprid		C ₉ H ₁₀ ClN ₅ O ₂	255.7	610	0.57
Clothianidin		C ₆ H ₈ ClN ₅ O ₂ S	249.7	327-340	0.70-0.91
Thiamethoxam		C ₈ H ₁₀ ClN ₅ O ₃ S	291.7	4100	-0.13

Acetamiprid		C ₁₀ H ₁₁ ClN ₄	222.7	2950	0.80
Dinotefuran		C ₇ H ₁₄ N ₄ O ₃	202.2	39830	-0.55
Nitenpyram		C ₁₁ H ₁₅ ClN ₄ O ₂	270.7	570000 (extremely high)	-0.66

*Water solubility values reflect typical solubility under ambient lab conditions (20 °C, pH=7)

Table 2. Regulatory variability of MRLs in mg/Kg for selected NEO across food commodities and jurisdictions.

Compound	Apple (pome fruit)	Tomato (fruiting veg)	Lettuce (leafy veg)	Grape (table/wine)	Honey	Ref.
Imidacloprid	0.05–1.0	0.05–0.5	0.1–1.0	0.05–0.5	0.02–0.1	(Authority et al. 2019)
Thiamethox am	0.01–0.3	0.02–0.4	0.05–0.4	0.01–0.2	0.01–0.05	(Almeida et al. 2025)
Clothianidin	0.01–0.5	0.01–0.3	0.05–0.5	0.01–0.2	0.01–0.05	(Ahn et al. 2022)
Acetamiprid	0.01–0.2	0.02–0.3	0.05–0.30	0.01–0.15	0.01–0.03	(Du et al. 2020)
Dinoteturan	0.01–0.1	0.01–0.1	0.01–0.1	0.01–0.08	0.01–0.03	(Ding et al. 2023)
Nitenpyram	0.01–0.05	0.01–0.05	0.01–0.05	0.01–0.04	0.01–0.02	(Kammoun et al. 2019)

Table 3. Performance comparison of analytical workflows for NEO residue determination in food matrices.

Method	Matrix	Target NEOs	Typical LOQ/LOD	Cleanup materials	Typical sample prep time / throughput (per sample)	Ref.
Modified QuEChERS combined with LC–MS/MS	Tomato, apple, leafy veg	Imidacloprid, clothianidin, thiamethoxam (multi-residue panels)	LOQ typically 0.001–0.01 mg/kg (method-dependent; many studies report 0.01 mg/kg reporting limit consistent with SANTE guidance)	d-SPE with PSA, C18, and GCB; matrix-matched calibration; isotopic ISTDs often used	30–60 min sample preparation (parallel batches increase throughput)	(Li et al. 2019) (De Mastro et al. 2022)
QuEChERS adapted for honey combines with LC–MS/MS/GC–	Honey (high-sugar)	Wide multiresidue including NEOs (imidacloprid,	Reporting limit / LCL 0.01 mg/kg (SANTE-compliant reporting limit	d-SPE with PSA C18; freezing-out step or dilution to reduce sugar; use of enzyme	45–90 min per sample (depends on freezing/centrifuge steps); high	(Lasheras et al. 2021)

MS/MS for 399 pesticides		acetamiprid, clothianidin)	used in study); recoveries 70–120%	pretreatment optional	throughput from batching	
DES-assisted DLLME (green DLLME)	Vegetable oil & concentrated extracts (adaptable to diluted fruit/juice extracts	acetamiprid, imidacloprid, thiacloprid, thiamethoxam	LOD 0.4–4.95 ng/μL; LOQ 1.43–9.70 ng/μL (reported as ng/μL in extract). Converted depending on final extract volume commonly achieves sub-μg/kg equivalent sensitivity after concentration	Choline chloride; ethylene glycol as extraction solvent; green solvent, high preconcentration factors (39–118)	5 minutes extraction with centrifuge/phase-separation; low-time microextraction (fast)	(Sengane et al. 2024)
MSPE-magnetic MWCNTs / Fe ₃ O ₄	Honey	NEOs (multi-pesticide panels)	Reported LOQs in the low ng/g (often <0.01 mg/kg) range after enrichment; typical recoveries ≥80%	Magnetic MWCNTs, Fe ₃ O ₄ -MIP, polymeric magnetic sorbents; selective sorbents shorten cleanup and minimise sugar adsorption	10–30 min extraction with magnetic separation; enrichment, amenable to automation	(Ding et al. 2023) (Fathi et al. 2023)
SPME / HS-SPME (fiber coatings). SPME used mainly for volatiles or pre-screening; recent coatings extend applicability	Honey (headspace) or diluted fruit extracts	best for semi-volatile pesticides and volatile degradation products; less suited for polar NEOs without derivatisation	LOQs vary widely; often ng/g level but reproducibility lower than solvent-based methods - useful for screening	Fiber chemistries (PDMS, DVB/CAR/PDMS, ionic-liquid coatings) and thermal desorption to GC-MS	10–60 min per sample (equilibration, adsorption, and desorption); lower throughput unless automated autosamplers used	(Kerkich et al. 2024)

Table 4. Characteristics and application potential of rapid screening technologies for NEO monitoring.

Detection platform	Target analytes	Matrix tested	Sample preparation	Detection principle / format	Reported LOD/LOQ	Assay time	Advantages	Limitations	Field applicability	Ref.
LFIA	Imidacloprid	Fruits, berries, agricultural products	Simple extraction with buffer solution; dilution before analysis	Competitive immunochromatographic assay using antibody–label conjugates	ng/mL range ($\approx$ μ g/kg depending on matrix)	5–15 min	Rapid, low cost, visual interpretation, minimal equipment	Antibody cross-reactivity; matrix interference; mainly semi-quantitative	High; suitable for preliminary field screening	(Barshevs kaya et al. 2025)
Phage peptide-based immunoassay	Imidacloprid	Agro-products and environmental samples	Extraction followed by dilution	Competitive immunoassay using phage-borne peptides as recognition elements	ng/mL level	<30 min	High sensitivity; alternative recognition strategy; low reagent requirement	Limited commercial availability; requires validation for different food matrices	Moderate; potential for portable screening	(Du et al. 2020)
Electrochemical aptasensor	Imidacloprid, thiamethoxam, clothianidin	Food samples	Extraction and filtration/dilution	Nanomaterial-modified electrode with electrochemical signal amplification	Low nM range	10–30 min	Portable, low sample volume, potential smartphone integration	Electrode fouling; matrix effects; requires calibration	High; suitable for portable readers	(Almenha li et al. 2025)
Electrochemical nanomaterial sensor	Imidacloprid	Food and environmental samples	Minimal extraction depending on matrix	WS ₂ nanosheet-modified electrode with voltammetric detection	Sub- μ M to nM range	<20 min	Simple operation, rapid response, low cost	Limited multiplex capability; affected by interfering compounds	Moderate–high for field screening	(Haritha et al. 2023)
SERS	Imidacloprid, thiamethoxam, clothianidin	Agricultural products, food matrices	Extraction followed by SERS	Raman molecular fingerprint enhancement using nanostructured substrates	ng/mL– μ g/kg range depending	Minutes	High chemical specificity, rapid	Signal reproducibility, substrate variation,	Moderate; suitable for portable	(Abu Bakar et al. 2024)

			substrate application		on substrate		detection, minimal reagents	matrix fluorescence	Raman devices	
Magnetic molecularly imprinted polymer–SERS	Multiple neonicotinoids	Agricultural products	Magnetic extraction and enrichment	Molecular recognition combined with SERS fingerprint detection	Low µg/kg range	<30 min	Improved selectivity and enrichment; suitable for complex matrices	Requires specialized substrates and validation	Moderate; promising for field-deployable systems	(Cao et al. 2024)
Paper-based analytical device / microfluidic platform	Neonicotinoid pesticides	Food and environmental samples	Integrated extraction and detection on chip	Microfluidic separation combined with colorimetric/electrochemical detection	ng/mL–µg/kg range	10–60 min	Low solvent consumption, portable, disposable, suitable for resource-limited areas	Lower sensitivity than laboratory instruments; difficult matrix cleanup	High potential for decentralized monitoring	(Agrawal et al. 2022)
Smartphone-assisted optical detection	Selected NEOs (mainly imidacloprid)	Food extracts and environmental samples	Simple extraction and image acquisition	Smartphone camera-based colorimetric/optical signal analysis	Depends on sensor platform	Minutes	Data recording, geolocation, remote monitoring capability	Requires standardized imaging conditions and validation	High potential for smart surveillance networks	(Luo et al. 2022)

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843 **Table 5.** Matrix-driven analytical challenges and mitigation strategies for LC–MS-based NEO residue analysis.

Matrix		Typical interfering classes		Example effect on LC-MS/MS	Practical mitigation	Ref.
Honey		Sugars,	pollen	Strong ion suppression; viscous deposits	SPE (HLB/mixed-mode), ILIS, dilution, matrix-matched calibration	(Visconti G. et al. 2024) (Oymen et al. 2022)
Leafy veg (lettuce, spinach)		Chlorophyll,	lipids, pigments	Severe suppression and column contamination	QuEChERS + GCB/EMR-lipid, longer gradients, ILIS	(FerrariSpeltini 2023) (Yang et al. 2023)
Fruiting (tomato)	veg	Sugars,	organic acids	Moderate suppression at early RT	Buffered extraction, PSA/C18 cleanup, matrix-matched calibration	(Yang et al. 2023)
Fruit peel (apple, citrus)		Waxes,	pigments, pectin	Peak tailing, source fouling	Peel-specific cleanup, solvent exchange, source maintenance	(FerrariSpeltini 2023)

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