

## ADVANCED FOOD CHEMISTRY — A NARRATIVE REVIEW

*Narrative Review*

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### ABSTRACT

**Background:** The chemistry of food processing governs both the sensory appeal and safety of what we consume. While reactions like the Maillard process and lipid oxidation contribute to desirable flavors and textures, they are also responsible for generating compounds with potential toxicological significance, such as advanced glycation end products (AGEs) and reactive aldehydes. Simultaneously, emerging non-thermal technologies and high-resolution analytical techniques are transforming how these processes are monitored and optimized.

**Objective:** This narrative review aims to consolidate recent advancements (2022–2025) in the chemical, analytical, and technological dimensions of food processing, with an emphasis on flavor development, safety, and nutritional quality.

**Main Discussion Points:** The review is structured around five thematic domains: (i) the mechanistic formation and dietary implications of Maillard reaction products and AGEs; (ii) lipid oxidation and its interplay with protein degradation; (iii) non-thermal processing techniques such as cold plasma and pulsed electric fields (PEF), and their molecular impacts; (iv) foodomics and the application of high-resolution mass spectrometry (HRMS) for targeted, suspect, and non-targeted screening; and (v) flavor chemistry, with a focus on advanced analytical tools including GC×GC-MS, PTR-ToF-MS, and chemometrics. Each section offers mechanistic insights, typical concentration ranges, analytical best practices, and practical decision-making frameworks.

**Conclusion:** The integration of advanced processing technologies with robust analytical workflows presents new opportunities to balance sensory quality with safety. However, standardized methodologies and real-world validation are essential to translate laboratory findings into applied food systems.

**Keywords:** Maillard reaction, advanced glycation end products (AGEs), lipid oxidation, foodomics, non-thermal processing, high-resolution mass spectrometry (HRMS).

## INTRODUCTION

The chemical and physical transformations that govern food quality, stability, and safety are inherently complex and dynamic, influenced by a wide range of intrinsic and extrinsic factors. Among the most critical of these are heat, oxygen, light, enzymatic activity, and reactive species such as reactive nitrogen species (RNS) and reactive oxygen species (ROS) (1,2). These elements, individually and in synergy, drive oxidation, degradation, and structural modifications in food matrices, ultimately impacting nutritional value, sensory attributes, shelf life, and safety. The global food supply chain, marked by increasing demand for minimally processed, nutrient-dense, and microbiologically safe food, necessitates a deeper understanding of these chemical transformations and their broader implications. Traditional thermal processing, long regarded as the gold standard for ensuring microbial safety, often comes at the cost of degrading thermolabile nutrients and altering sensory properties (3,4). In recent years, however, there has been a significant shift toward the adoption of non-thermal technologies such as high-pressure processing (HPP), pulsed electric fields (PEF), cold plasma, and ultraviolet (UV) treatment. These novel approaches promise to decouple microbial inactivation from thermal damage, thereby preserving food quality while ensuring safety (5,6). While promising, the molecular mechanisms underpinning these technologies remain underexplored, particularly with respect to how they influence food chemistry at the microstructural and metabolomic levels.

Simultaneously, the field of food analysis has undergone a transformation driven by advances in analytical instrumentation. High-resolution mass spectrometry (HRMS) coupled with multidimensional chromatography techniques now enables the detection of thousands of molecular features within a single sample (7). These analytical breakthroughs provide unprecedented resolution and depth in profiling food constituents, degradation products, contaminants, and markers of processing. However, the resulting data sets are highly complex and high-dimensional, posing significant challenges in interpretation and integration (8). Chemometric methods and non-targeted analytical strategies have become indispensable in decoding this wealth of information, yet the field continues to grapple with standardization, reproducibility, and biological relevance of the data generated. Despite these advancements, significant gaps persist in both mechanistic understanding and practical implementation (9,10). For instance, there remains limited clarity on which specific markers should be targeted to assess oxidative damage or microbial inactivation in foods subjected to emerging technologies. Moreover, inconsistencies in analytical methodologies and a lack of harmonization across studies hinder the development of universally accepted indicators for food quality and safety (11). There is also a pressing need to bridge the gap between mechanistic insight derived from advanced analytical techniques and actionable guidance that can be translated into routine quality control or regulatory frameworks.

The objective of this review is to synthesize current knowledge on the physicochemical transformations occurring in food under the influence of both conventional and emerging processing conditions, with an emphasis on oxidative reactions, enzyme-mediated changes, and the role of RNS and ROS. By drawing on the latest developments in HRMS, multidimensional chromatography, and chemometrics, this review aims to provide a practical roadmap for practitioners, researchers, and regulatory bodies (12,13). Specifically, it discusses what analytes and molecular markers should be measured, the rationale for their selection, and the most appropriate analytical approaches to employ. The review also addresses how different processing technologies—particularly non-thermal methods—modulate these markers, and what implications these changes have for food safety, nutritional value, and consumer acceptability. In conducting this review, emphasis is placed on studies employing non-targeted metabolomic approaches and advanced data processing techniques, as well as those that provide mechanistic insights into the underlying chemistry of food transformation. Priority is given to literature that incorporates high-throughput or high-resolution methods capable of resolving complex food matrices. Studies that link chemical markers with sensory attributes, nutritional outcomes, or microbial stability are particularly highlighted, as they offer the most direct relevance to food quality assessment and product development. This review is both timely and necessary, given the accelerating pace of innovation in food processing and the parallel rise in consumer demand for high-quality, safe, and minimally processed products. By integrating mechanistic knowledge with analytical best practices, this work contributes novel insights that can inform the design of safer and more sustainable food systems. Moreover, it provides actionable recommendations that can guide practitioners in selecting appropriate analytical tools and interpreting complex data sets for decision-making. The review thus fills a critical gap at the intersection of food chemistry, analytical science, and process engineering, offering a comprehensive and practically oriented resource for the field.

## MAILLARD CHEMISTRY & DIETARY AGES

### Mechanistic overview

The Maillard reaction, a non-enzymatic interaction between reducing sugars and amino compounds, underpins both flavor development and the formation of advanced glycation end-products (AGEs) in thermally processed foods. Initially, this reaction forms a Schiff base that rearranges into Amadori or Heyns products, which then undergo a complex series of reactions—including fragmentation, dehydration, and oxidation—to yield reactive dicarbonyls like methylglyoxal and glyoxal, as well as stable end-products such as N $\epsilon$ -carboxymethyllysine (CML), N $\epsilon$ -carboxyethyllysine (CEL), and pyrraline. These processes are highly sensitive to variables such as temperature, water activity, pH, and the presence of catalytic metal ions (1). The reaction also produces compounds with health implications, including acrylamide, furans, and heterocyclic amines (2,3).

### Quantitative markers and typical ranges

Typical concentrations of key Maillard reaction markers vary depending on matrix and processing conditions. For example, CML levels in thermally processed cereals range from 10–150 mg/kg protein, while CEL in roasted meats may span 5–80 mg/kg. Acrylamide concentrations are highly variable in baked and fried foods, often falling between 50 and 3000  $\mu$ g/kg. Similarly, furan levels in retorted foods and beverages may exceed 100  $\mu$ g/kg. These markers are not only useful for assessing exposure but also serve as indirect indicators of process intensity and potential toxicological concerns (4).

### Analytical methods (best practice snapshot)

Robust analytical workflows are essential for quantifying Maillard reaction products. Stable isotope dilution analysis (SIDA) using LC-MS/MS is considered the gold standard for quantifying CML, CEL, and pyrraline after enzymatic hydrolysis and solid-phase extraction. Acrylamide quantification typically relies on LC-MS/MS with isotopically labeled standards, with GC-MS employed as a confirmatory technique post-derivatization. Derivatization of reactive carbonyls (e.g., methylglyoxal) with o-phenylenediamine allows for subsequent LC-MS/MS analysis of quinoxaline derivatives. Non-targeted high-resolution mass spectrometry (HRMS) further contextualizes these products within broader chemical profiles of thermally processed foods (5).

### Exposure and mitigation

Epidemiological and interventional studies indicate that high-AGE diets, especially those involving dry-heat cooking methods like grilling and roasting, contribute to elevated serum AGE levels and inflammatory biomarkers. Practical mitigation strategies include switching to moist-heat techniques (e.g., steaming), reducing cooking temperature and time, incorporating acidic marinades, and using enzymatic interventions such as asparaginase to limit acrylamide formation. Though promising, the effects on metabolic endpoints like glycemia and lipid profiles remain modest and heterogeneous (6).

## LIPID OXIDATION & PROTEIN–LIPID CROSSTALK

### Mechanisms

Lipid oxidation occurs via autooxidation, photo-oxidation, or enzymatic routes. These pathways generate lipid hydroperoxides that decompose into aldehydes (e.g., hexanal, 4-HNE), ketones, and acids. These secondary products not only alter sensory attributes but can react with proteins, forming crosslinks and aggregates that compromise nutritional quality and bioavailability (7).

### Monitoring strategy

Monitoring involves both primary and secondary markers. Primary markers include peroxide value and conjugated dienes, while secondary indicators such as p-anisidine value and TBARS (measuring malondialdehyde) are more indicative of advanced oxidation. Volatile aldehydes can be quantified using SPME-GC-MS. Protein oxidation is often evaluated using DNPH for carbonyls, Ellman's reagent for sulfhydryls, and tryptophan fluorescence quenching. Advanced methods like LC-HRMS are increasingly used to identify aldehyde–amino acid adducts.

### Data table—volatiles indicative of lipid oxidation

Key volatiles indicative of oxidation include hexanal (green, grassy odor, marker for n-6 PUFA oxidation), (E)-2-nonenal (cardboard-like odor, marker of advanced oxidation), and 4-HNE (pungent odor, derived from  $\omega$ -6 PUFA breakdown). These serve not only as analytical targets but also as sensory off-note markers in quality control applications.

### **Control levers**

Effective strategies to limit lipid oxidation include the use of antioxidants (e.g., tocopherols, polyphenols), metal chelators, and packaging barriers against oxygen and light. Food formulation also plays a role, with moisture reduction in snacks and emulsion design affecting oxidation kinetics. Interfacial engineering using proteins and polysaccharides can enhance oxidative stability (8,9).

## **NON-THERMAL PROCESSING CHEMISTRIES**

### **Cold Plasma (CP)**

Cold plasma utilizes ionized gas species including hydroxyl radicals, ozone, and nitric oxide to inactivate microbes and degrade enzymes on food surfaces. While primarily used for surface decontamination, higher doses can lead to mild lipid oxidation and pigment modification. Crosslinking in proteins and polysaccharides has been noted, though typically without detrimental nutritional impact.

### **Pulsed Electric Fields (PEF)**

PEF applies high-voltage pulses to induce electroporation in microbial cells, enhancing safety without thermal degradation. It also facilitates mass transfer, improving extraction of bioactives and aroma precursors. In protein-rich matrices, structural changes may improve solubility and functionality. Processing outcomes depend on matrix properties such as pH and ionic strength.

### **Comparative decision matrix**

Cold plasma excels in surface treatment and enzyme inactivation with minimal nutrient loss at optimized doses. PEF is more suited for microbial control and enhancement of extractable flavor and nutrient compounds. Analytics typically involve LC-MS for oxidation products, fluorescence-based assays for protein changes, and GC-MS for volatile profiles.

## **FOODOMICS & HRMS WORKFLOWS (TARGETED → SUSPECT → NON-TARGETED)**

### **Tiered strategy**

Foodomics employs a three-tiered approach: targeted analysis for compliance (e.g., CML, acrylamide); suspect screening based on exact mass and fragmentation; and non-targeted screening (NTS) for discovery of unknowns using high-resolution MS and in silico tools. This workflow bridges routine quality control and exploratory research.

### **Practical NTS prioritization**

NTS requires careful sample pairing (pre- and post-processing), use of Kendrick mass defect tools, and filtering by internal standard response and toxicological concern (AET/TTC). Quality assurance involves procedural blanks, matrix spikes, and spectral libraries, with growing emphasis on open-access metadata.

### **Emerging areas**

Emerging technologies such as proton transfer reaction (PTR-ToF-MS) and selected ion flow tube (SIFT-MS) enable real-time volatile tracking. GC×GC-MS/Olfactometry enhances resolution of co-eluting compounds, while machine learning models are being integrated for pattern recognition and risk prediction in food safety contexts (10,11).

### **Flavor Chemistry—From Formation to Sensing**

#### **Pathways & formation**

Flavor compounds arise from the interplay of Maillard chemistry, lipid oxidation, fermentation, and thermal degradation. Key intermediates include Strecker aldehydes, sulfur heterocycles, and lactones. Reaction trajectories are governed by matrix parameters such as water activity and redox potential (12).

## Modern analytical toolbox

Modern flavor analysis utilizes GC×GC-MS for comprehensive volatile mapping and GC-Olfactometry (GC-O) for sensory relevance. PTR-ToF-MS and SIFT-MS offer real-time process monitoring. Chemometric models are used to link volatile fingerprints with sensory perceptions and consumer preferences.

## Data table—high impact odorants (examples)

High-impact odorants include 2/3-methylbutanal (Maillard, ODT: 0.1–1 ppb), 2-furanmethanethiol (roasted sulfur notes, ODT ~0.004 ppb), and (E)-2-nonenal (oxidation, ODT: 0.1–1 ppb). These compounds are critical for both quality assurance and flavor design.

## Method Selection Guide (Quick Use)

A strategic approach to analytical method selection ensures actionable insights. For acrylamide mitigation, combine LC-MS/MS quantification with tracking of precursors (asparagine, sugars) and browning markers (CML/CEL). For off-flavor investigation, rapid screening by PTR-MS followed by GC×GC-MS/O and sensory validation is recommended. Unknown packaging migrants should be analyzed by NTS with risk prioritization and subsequent targeted confirmation.

# CRITICAL ANALYSIS AND LIMITATIONS

The growing body of literature on Maillard chemistry, lipid oxidation, and non-thermal food processing has advanced the understanding of flavor formation, oxidative stability, and food safety. However, a critical appraisal reveals several methodological and interpretive limitations that constrain the generalizability and practical utility of these findings. One of the primary concerns is the widespread reliance on in vitro model systems rather than real food matrices. Many studies simulate reactions using simplified mixtures of amino acids, sugars, or fats under controlled laboratory conditions, which do not fully replicate the complexity of industrial or culinary settings. For instance, while the role of chicken fat in Maillard reaction enhancement has been demonstrated in peony seed-based systems (13-15), the results may not directly translate to whole food matrices where water activity, endogenous enzymes, and food structure influence outcomes. This over-reliance on model systems can lead to oversimplification and a limited understanding of reaction kinetics and intermediate pathways in complex foods. Additionally, a common limitation across many studies is the lack of standardization in analytical methodologies. Different research groups employ varying extraction methods, derivatization protocols, and detection systems (e.g., GC-MS vs. LC-MS), making cross-study comparisons difficult. For example, while lipid oxidation markers such as hexanal and 4-HNE are routinely used, the threshold levels defining sensory rejection or toxicity are inconsistently reported. Similarly, the methods used to quantify antioxidant activities of Maillard reaction products (MRPs) vary in sensitivity and relevance to actual in vivo outcomes (16,17). This methodological heterogeneity introduces significant bias and reduces the reproducibility of findings. Confounding factors are also poorly controlled in many investigations. For example, studies examining lipid–Maillard interactions often fail to isolate the effects of oxidation products from those of native lipids or processing variables like time and temperature. In a study investigating flavor development in mussel MRPs, both polar and nonpolar lipids influenced volatile profiles, yet the contribution of lipid oxidation alone was difficult to isolate due to overlapping reaction pathways (18,19). Moreover, sensory analysis is often conducted using untrained panels or lacks detailed descriptions of panel size, calibration, and inter-rater reliability, leading to potential performance bias.

Another critical issue is the underreporting of null or inconclusive results, suggesting potential publication bias. The literature is heavily skewed toward studies showing desirable flavor formation, antioxidant activity, or improved oxidative stability following Maillard or non-thermal treatments. There is relatively less representation of studies highlighting off-flavor generation, degradation of nutritional quality, or failure to achieve microbial targets. For instance, despite the promising antioxidative effects of MRPs, their negative impact on essential amino acid availability or potential pro-oxidant activity at high concentrations is rarely discussed (20). Variability in outcome measures further hampers meta-analysis and synthesis. Studies often assess different markers of Maillard reactivity or oxidation—ranging from browning intensity and fluorescence to specific molecular adducts—without standard endpoints. Moreover, antioxidant activity is assessed using diverse in vitro assays (e.g., DPPH, ABTS, FRAP) with limited correlation to biological efficacy. These inconsistencies make it difficult to draw robust conclusions about the functional benefits or risks of MRPs and lipid-derived compounds across food systems. Generalizability also remains a major challenge. Most studies focus on specific ingredients, such as chicken fat, flaxseed, or rice protein, and their interaction within narrow model contexts. The applicability of these findings to broader food categories (e.g., dairy, beverages, emulsified products) is questionable. For instance, a study exploring the effect of unsaturated aldehydes on the flavor profile of glutathione–ribose MRPs observed significant changes in sensory perception, but it is unclear how

such effects translate to meat or dairy applications with vastly different matrices (21). Furthermore, regional culinary practices, ingredient variability, and consumer preferences introduce cultural dimensions that are seldom addressed in experimental designs. In conclusion, while advances in analytical chemistry and foodomics have deepened mechanistic insights into Maillard reactions, lipid oxidation, and non-thermal food processes, substantial limitations persist in study design, methodological rigor, and interpretive transparency. Addressing these gaps through standardized protocols, real food validations, and better reporting of negative results will be critical for translating laboratory findings into meaningful improvements in food quality, safety, and sensory performance.

## IMPLICATIONS AND FUTURE DIRECTIONS

The synthesis of current literature on Maillard chemistry, lipid oxidation, and non-thermal processing offers valuable translational insight not only for food scientists and technologists but also for stakeholders in nutrition, public health, and regulatory frameworks. The evolving understanding of how advanced glycation end-products (AGEs), lipid oxidation products, and flavor-active volatiles form and interact during processing has meaningful implications for dietary health. Specifically, recognizing the links between high-AGE diets and systemic inflammation suggests that culinary practices in institutional and clinical nutrition—such as in hospitals or long-term care—should prioritize cooking techniques that minimize dry-heat exposure and favor steaming, stewing, or sous-vide methods, which have been shown to reduce AGE burden without compromising palatability (22). In terms of policy and food safety regulation, the findings highlight a pressing need for updated guidelines that address not only microbial risks but also chemical safety associated with modern food processing. Despite growing awareness of potentially harmful compounds like acrylamide, 4-HNE, or methylglyoxal, there is insufficient harmonization across jurisdictions on acceptable thresholds or mandatory labeling. Policymakers could leverage insights from non-targeted screening (NTS) workflows to better define monitoring requirements and risk thresholds based on high-resolution exposure data. However, this would require the establishment of standardized reporting frameworks for NTS, including clear levels of compound identification and access to curated spectral repositories that ensure reproducibility and inter-laboratory comparability (23,24). Numerous research gaps remain unaddressed. While the antioxidant potential of Maillard reaction products has been established in vitro and in model foods, their in vivo effects—particularly their interactions with endogenous metabolic pathways—are poorly understood. Similarly, studies exploring flavor formation often overlook the long-term nutritional consequences of advanced processing methods, including nutrient loss, bioavailability changes, and potential allergenicity due to protein cross-linking. There is also limited investigation into the synergistic effects between Maillard products and lipid oxidation in complex matrices like emulsions or mixed meals. Understanding these interactions is critical for accurately modeling both health risks and sensory outcomes (25).

Future studies should adopt more holistic and process-aware designs. Digital twin modeling—virtual simulations that integrate mass transfer, reaction kinetics, and microbial inactivation—could help optimize processing parameters that balance flavor enhancement with safety and nutritional retention. In parallel, more work is needed on green analytical techniques, such as microextraction, ambient ionization, and solvent-free approaches compatible with high-resolution mass spectrometry. These advancements would support scalable, environmentally sustainable monitoring of chemical markers across food systems (26). Methodologically, there is a strong case for transitioning from simple binary model systems to more physiologically relevant matrices. Future research should prioritize factorial designs incorporating different ingredient combinations, cooking conditions, and storage environments, analyzed using untargeted omics platforms. Moreover, interdisciplinary approaches that combine chemical analytics, sensory science, and nutritional biomarkers would yield more comprehensive insights. Multicenter trials that compare AGE or oxidation marker loads in foods prepared under varied domestic and industrial conditions could also bridge the gap between mechanistic data and real-world exposure. In conclusion, the implications of Maillard and lipid oxidation chemistry extend far beyond the laboratory, touching on clinical nutrition strategies, public health policies, and the future of sustainable food design. Aligning analytical advances with regulatory needs and consumer health priorities will require a concerted effort across scientific, industrial, and policy domains.

## CONCLUSION

This review has synthesized current understanding of Maillard chemistry, lipid oxidation, and non-thermal food processing, emphasizing their intertwined roles in shaping food quality, flavor, safety, and nutritional value. Key findings highlight that while Maillard-derived compounds contribute to desirable sensory attributes, they also generate dietary AGEs and contaminants that may pose health risks. Lipid oxidation, particularly when unchecked, leads to the formation of volatile aldehydes and protein modifications that compromise both flavor and biofunctionality. Non-thermal technologies such as cold plasma and pulsed electric fields offer promising alternatives

to conventional processing by minimizing thermal damage while maintaining microbial safety, though their long-term chemical effects require deeper evaluation. The strength of current evidence is notable in its mechanistic depth and analytical sophistication; however, gaps in standardization, real-world validation, and long-term health implications limit broad application. Practically, researchers and food professionals should prioritize harmonized analytical approaches, process-aware modeling, and green technologies that align safety with sensory excellence. Ultimately, there is a critical need for well-designed, matrix-specific studies that integrate chemical profiling, sensory science, and human health outcomes to bridge the laboratory and the plate.

**AUTHOR CONTRIBUTION**

| Author                | Contribution                                                                                                                                                                          |
|-----------------------|---------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| Muhammad Usama Aslam* | Substantial Contribution to study design, analysis, acquisition of Data<br>Manuscript Writing<br>Has given Final Approval of the version to be published                              |
| Esha Aslam            | Substantial Contribution to study design, acquisition and interpretation of Data<br>Critical Review and Manuscript Writing<br>Has given Final Approval of the version to be published |
| Muhammad Shahbaz*     | Substantial Contribution to acquisition and interpretation of Data<br>Has given Final Approval of the version to be published                                                         |

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