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Review

Nanostrategy for Selective Ethyl Carbamate Removal from Fermented Alcoholic Beverages via Molecular Imprinting Technology

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Abstract: Ethyl carbamate (EC), known as urethane, is a naturally occurring potentially carcinogenic metabolite that is widely found in alcoholic beverages and other food-related fermented products. The concern related to the presence of the EC and its toxicity in regularly consumed fermented alcoholic beverages raises global interest in assessing the possible risks to human health. EC mitigation approaches, such as molecular imprinting technology (MIT), have been proposed to target EC while preserving the sensory quality of fermented alcoholic beverages. This review explores the principles of MIT, the advantages and disadvantages of the most common polymerisation approach for molecularly imprinted polymer (MIP) synthesis, the analytical techniques used for MIP characterisation, and the strategies used to mitigate EC in fermented alcoholic beverages, with studies reporting removal efficiencies of up to 84%. Additionally, it highlights the novelty and potential of MIPs, offering practical insights into their integration within the production of fermented alcoholic beverages, highlighting their scalability and cost-effectiveness compared to traditional EC mitigation strategies.

Keywords: ethyl carbamate; fermented alcoholic beverages; molecularly imprinted polymers; synthesis; characterisation; applications

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1. Introduction

Food safety is a worldwide concern, regardless of foodborne diseases and economic and social development, and it is a priority for global governmental programs. Food safety is a public–private partnership among industry, government, academia, and the consumer to address public health requirements and questions concerned with nutrition, health, food science, and ingredient safety [1]. According to the Center for Disease Control and Prevention, each year in the United States, 48 million people get sick, 128,000 are hospitalised, and 3000 die due to foodborne diseases [2]. Therefore, the study of toxic and carcinogenic substances in foods represents one of the most demanding areas in food safety due to their repercussions for public health. Moreover, their presence represents an obstacle of high relevance for product exportation, which has a devastating economic impact on the food industry.

Contaminants in food can be classified based on their origin and nature. These can be microbiological (e.g., bacteria, parasites), extraneous matter (e.g., biological, chemical), natural toxins (e.g., mycotoxins), other chemical compounds (e.g., pesticides, toxic metals, undesirable fermentation products), packaging materials, and poisons introduced through tampering. These contaminants can lead to serious health issues, particularly illnesses related to drug resistance that reduce the efficacy of medicines [3]. In addition, the maximum

levels allowed in foods are governed by regulatory limits monitored by the national health authorities in order to eradicate the risk for the consumer.

Ethyl carbamate (EC), often known as urethane, is a naturally occurring chemical present in several fermented alcoholic beverages (e.g., wine, beer, liquor, brandies). EC can be formed primarily through the reaction between urea and ethanol, which is influenced by fermentation conditions (e.g., pH, levels of urea or citrulline, ethanol level), yeast metabolism (e.g., some wine yeasts generate more urea as a byproduct of nitrogen metabolism), and storage practices. Additionally cyanogenic glycosides and ethyl carbamyl phosphate can contribute to EC formation under specific conditions, with copper ions (Cu^{2+}) enhancing cyanate production, as shown in Figure 1 [4–7].

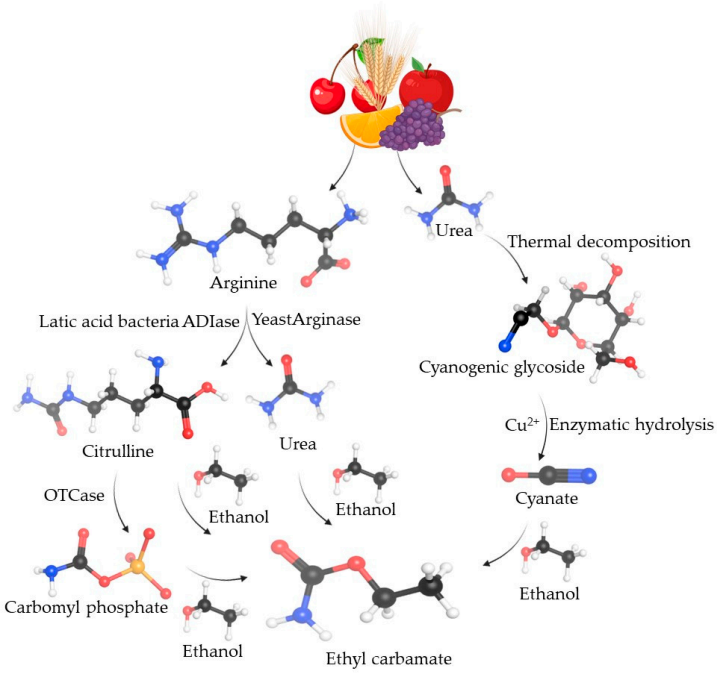


Figure 1. Main mechanisms involved in ethyl carbamate (EC) formation in fermented alcoholic beverages.

Apprehension related to EC occurrence in fermented alcoholic beverages arose in 1985, when relatively high levels were detected by Canadian authorities in wines and other liquors. Health authorities have identified it as a potential carcinogen, leading to international efforts to limit its levels in fermented alcoholic beverages. The International Agency for Research on Cancer classified EC as a Group 2A carcinogen, suggesting it is "probably carcinogenic to humans" based on suitable assays of carcinogenicity in animals. The World Health Organization, a global regulatory authority, has established recommended guidelines for EC levels in fermented alcoholic beverages. For instance, Canada set maximum limits (MLs) for EC in fermented alcoholic beverages according to consumption patterns and acceptable daily intake value evaluation: 30 µg/L for table wine, 100 µg/L for fortified wines, 150 µg/L for distilled spirits, and 400 µg/L for fruit dies and liquors [8–10]. The EU regulatory framework for this contaminant is evolving. Member states have not yet implemented enforceable MLs, but the European Commission has issued a recommendation setting a target value of 1 mg/L (EU Recommendation 2016/22) for monitoring purposes [11]. These limits are more commonly recommended rather than enforced limits. The Canadian Food Inspection Agency (CFIA) conducted a survey in 2022–2023 to examine EC levels in fermented foods available on the Canadian retail market, including alcoholic beverages. From 275 samples, including 181 fermented soy products and 94 wine samples, EC was detected in 34% of them, with concentrations ranging from 4 ppb to 824 ppb [12].

Moreover, in 2023, the review on EC concerning fermented food products showed that alcoholic beverages represent one current concern and require further monitoring and mitigation strategies [9]. Considering the health risks and regulatory attention, controlling EC levels in fermented alcoholic beverages is critical to ensure safety, marketability (avoiding trade restrictions), and quality (maintaining product quality and consumer trust).

Several traditional EC mitigation strategies have been proposed, such as metabolic engineering modification of yeast (e.g., enhancing the expressions of DUR3), enzymatic methods (e.g., adding acid urease), chemical (e.g., copper catalysts), and physical (e.g., charcoal filtration, distillation, low temperature, deoxygenated conditions, de-stoning process). Nonetheless, these traditional EC mitigation strategies demonstrate remarkable weaknesses, such as a deficit of selectivity and adverse effects on wine quality, as they can affect the wine's sensory properties (e.g., aroma, colour, taste), which are critical to its character and market value [13]. Subsequently, there is a requirement for more efficient strategies, like molecular imprinting technology (MIT), that can target EC while preserving the beverage's sensory quality. By combining the special properties of nanostructures with the molecular recognition power of an imprinted polymer, MIT and nanotechnology produce a material that is very sensitive and selective. To achieve remarkable specificity, MIT entails forming template-shaped voids in polymers that are complementary to a target molecule in terms of size, shape, and functional groups. Even trace-level analytes can be specifically detected and separated when used at the nanoscale (e.g., nanocomposites, nanoparticles, nanotubes), where the increased surface area and reactivity improve the recognition potential. With wide-ranging industrial and scientific applications, this synergy is a potent fusion of material science and molecular recognition, as shown in Figure 2, such as sensor technology (for detecting chemicals, drugs), drug delivery (can control the release by targeting precise therapeutic agents), sample treatment (use as a sorbent in the extraction procedure), and food safety (removal of contaminants), among others [14–18].

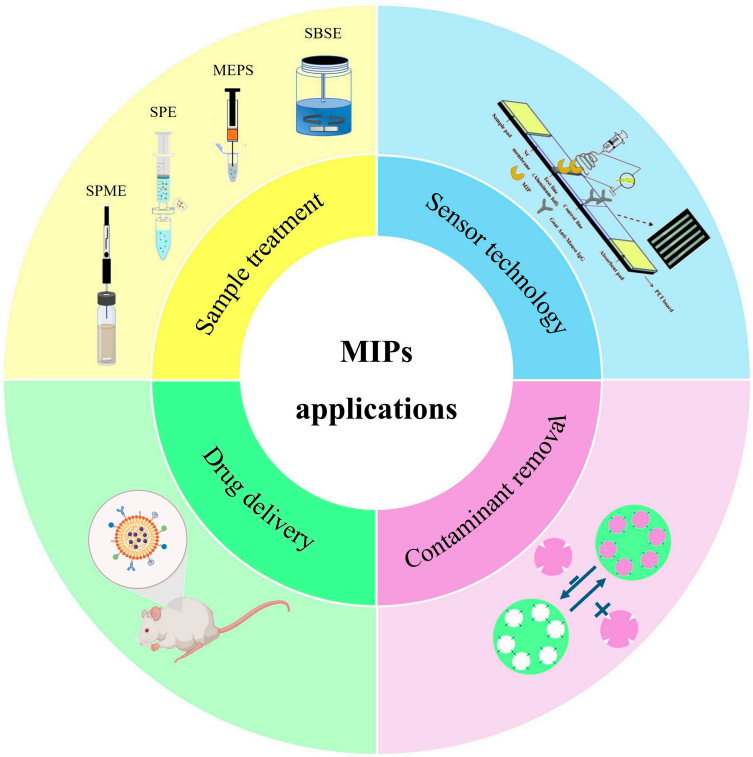


Figure 2. Potential molecularly imprinted polymer applications. Abbreviations: SPME—solid-phase microextraction; SPE—solid-phase extraction; MEPS—microextraction packed sorbent; SBSE—stir bar sorptive extraction.

The current review discusses the use of MIPs for removing EC from fermented alcoholic beverages (e.g., wines, beers, brandies, liquors) and the principles of MIT, MIP types, synthesis, and analytical techniques for MIP characterisation. In addition, this review not only highlights the novelty and potential of MIPs but also provides practical insights into their integration into fermented alcoholic beverage production.

2. Methods

This review took a retrospective approach, inspecting research articles from 2020 to 2024, concentrating on MIP applications to remove EC from fermented alcoholic beverages. Pertinent articles were located and chosen from the bibliographic databases Scopus, PubMed, and ScienceDirect for their widespread journal coverage. The selection criteria for these articles included title, abstract, keywords, and year of publication to identify the most current innovations in MIT for EC removal in potential industrial applications. Keywords applied in the search included "ethyl carbamate", "fermented alcoholic beverages", "wines", "liquor", "brandies", "molecularly imprinted polymers", "MIP synthesis", "MIP characterisation", and "MIP application." Additionally, wildcard symbols (*, $, etc.) and Boolean operators (AND, OR) were applied to improve search precision. By including all types of publications (e.g., articles, book chapters, reviews), the initial number of papers extracted contained nine duplicates, which were removed. Of the remaining 75 articles, they were grouped into the following categories: polymerisation method (e.g., bulk polymerisation, surface imprinting, suspension polymerisation), binding efficiency (adsorption capacity and binding affinity of the MIPs), selectivity, comparison with traditional removal strategies (e.g., activated carbon, enzymatic degradation), and application (e.g., wine, spirits, other fermented beverages). Of these, 12 were excluded due to insufficient data on MIP synthesis, characterisation, and application in EC reduction. In addition, non-peer-reviewed sources and studies that did not specifically address MIPs for EC mitigation were not included.

3. Molecularly Imprinted Polymers: Fundamentals and Mechanisms

MIT is the most popular nanoscience approach for creating MIPs, which are highly defined materials that can identify and attach to specific target molecules. This approach comprises polymerising functional monomers near a template molecule (EC or a structural analogue) in the presence of a cross-linking agent, stabilising the polymer matrix, hardening the structure, and fixing functional monomers' locations near the template molecule, as shown in Figure 3. When the polymerisation process is complete, the template molecule is retrieved, leaving cavities within the polymer matrix that match the template in forms of functional group arrangement (e.g., hydrogen bonds, ionic interactions, van der Waals forces, π-π interactions), shape, and size (EC "fit" precisely) that allow MIPs selectively recognise and bind the target molecule [19,20].

This elevated level of selectivity makes it an effective approach for removing EC from fermented alcoholic beverages. More specifically, a selective recognition and binding mechanism for EC means choosing a template molecule with similarities in the structure and functional groups of EC, therefore permitting a replica of binding sites specific to EC. With the addition of EC in MIP, it selectively binds within such sites through hydrogen bonding due to the presence of amino (NH_2) and carbamate (O=C-O) groups in the structure of EC, which are capable of forming hydrogen bonds with complementary groups inside the MIP cavity. Van der Waals and hydrophobic interactions sustain the stability of EC in the MIP binding site for higher selectivity. This specificity minimises the risk of binding to other components, thus preserving the sensory and chemical qualities of the fermented beverages being treated as a result of its stable structure and specific functional groups.

Usually, molecules that can form stable hydrogen bonds or hydrophobic interactions with EC, like methacrylic acid or acrylamide, are used to find the right functional monomers for EC-targeting MIPs. However, designing MIPs for small, uncharged molecules has some important difficulties: limited functional groups and lack of charge make their binding hardly selective since noncovalent interactions are weaker and less specific. Further optimisation of the polymer matrix for a stable, high-affinity binding site involves detailed studies of monomer–template ratios and conditions of polymerisation to avoid nonspecific interactions while developing an effective elution strategy that will remove the template post-polymerisation [21].

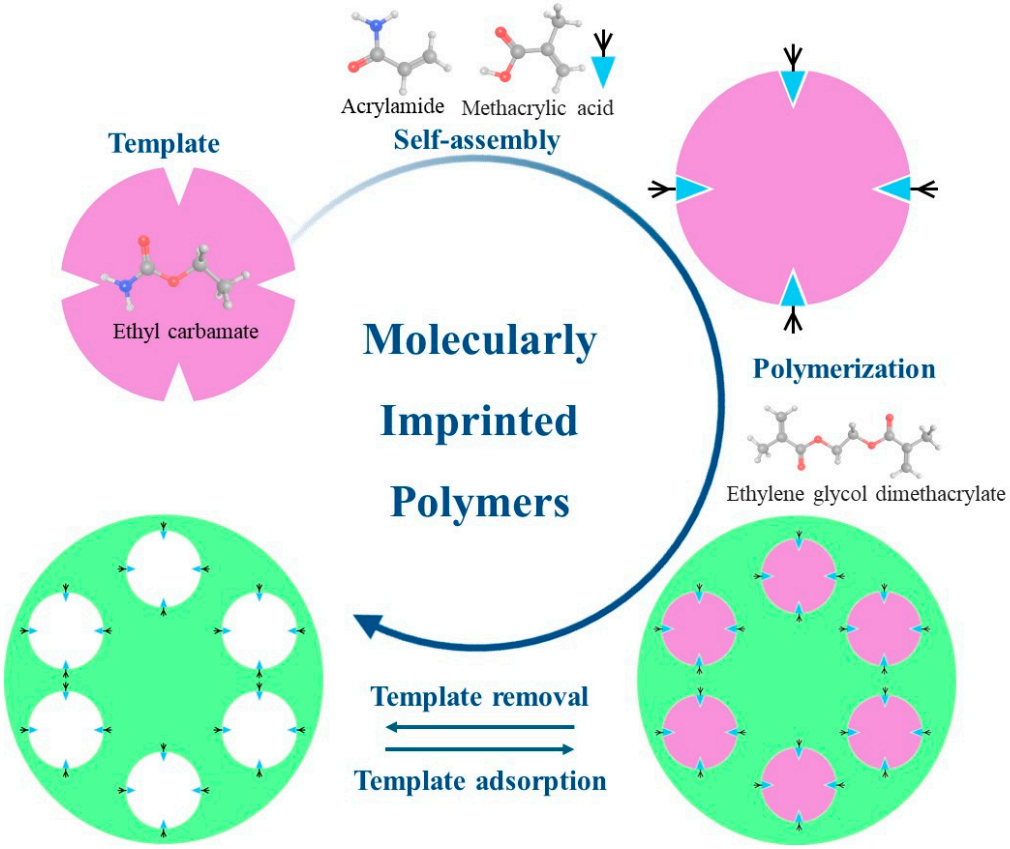
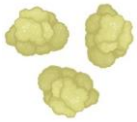
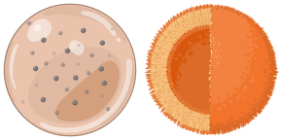
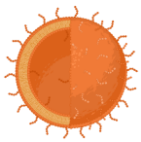


Figure 3. Imprinting technology of molecularly imprinted matrix using ethyl carbamate (EC) as a template.

Bulk polymerisation is the most widely used approach to synthesise MIPs, where the template molecules are mixed with monomers and cross-linkers to form a homogeneous polymer network. After the polymerisation process, grinding and sieving are required to create particles, which, while low-cost, produce irregularly shaped particles with an uneven distribution of binding sites, typically embedded deep within the polymer matrix. This decreases the accessibility of small molecules to the recognition sites, indicating slower binding kinetics and a lesser efficiency in analyte detection. This polymerisation method may also suffer from template leaching, compromising specificity and even posing a risk of contamination in sensitive analyses [19,20]. Suspension polymerisation is another frequently used approach for the synthesis of MIPs, wherein the monomer, crosslinker, and template are polymerised in an aqueous suspension to form spherical MIP beads. This method yields uniform microspheres from small colloidal droplets of the polymerisation mixture suspended in a liquid, often perfluorocarbon [20], but it may require additional steps to remove the template molecule fully, as shown in Table 1.

Table 1. Advantages and disadvantages of the most common polymerisation approach for MIP synthesis [17,22–26].

Polymerisation Approach	Advantages	Disadvantages
Bulk 	Easy Appropriate for the majority of polymer formulations Economical	Irregular size and shape Low reproducibility Effort and time consuming Lower binding kinetics
Suspension/emulsion 	Regular size and shape High reproducibility	Requires a stabiliser or a surfactant Solubility in a continuous phase
Precipitation 	No required stabiliser Regular size, shape, and morphology Popular for sensor applications	Aggregation Effort and time consuming
Sol–gel 	Preparation at room temperature High thermal and chemical stability Well-defined surface areas and porous structures Green solvents (water or ethanol)	Solubility of the template Lack of functional monomer
Core–shell particle 	Core can fulfil the function Binding sites are uniformly distributed Enhanced mass-transfer efficiency	Effort and time consuming More complex synthesis
Surface imprinting 	Enhanced mass-transfer efficiency Higher binding capacity Higher binding kinetics Lower embedding phenomena	Requires pure templates Recognition mechanism uncertain Use of noble metals is expensive Lower solubility of templates

A comparable approach is precipitation polymerisation, which is a refined form of bulk polymerisation, where the MIP forms as precipitated microspheres without grinding. It provides better control over particle size and shape and is suited for high-affinity binding in homogeneous conditions due to the addition of a porogenic solvent in the pre-polymerisation mixture [19,27]. Baggiani et al. [21], via bulk polymerisation using acrylamide and methacrylic acid as functional monomers, prepared two types of MIPs for the selective recognition and capture of EC. The experimental results show that methacrylic acid is much better than acrylamide as a functional monomer for achieving higher imprinting factors. In emulsion polymerisation, a biphasic system is created by suspending the pre-polymerisation mixture, which includes an initiator (polar phase), in a non-polar oily solvent with the aid of a surfactant [19]. The surfactant acts here as a template and promotes spherical micellar MIPs. This approach strongly increases the surface area, which is very popular nowadays in sensor applications. Because the sol–gel process involves inorganic materials or organic–inorganic network structures and no organic monomers, there are possibilities for simple preparation at room temperature and under conditions without using

organic solvents; this means water can be employed. This approach provides high thermal and chemical stability, making it suitable for environmental and high-temperature applications, and it results in MIPs with well-defined surface areas and porous structures [28]. Zheng et al. [26] propose a sol–gel approach to grow perovskite-structured lanthanum manganate ($LaMnO_3$) on graphene oxide, creating a nanocube-structured material with high electrocatalytic activity and a large surface area for EC detection in Baijiu. Another smart approach to synthesising MIPs is surface imprinting, which creates binding sites on the surface of materials, often by grafting or attaching the template directly onto a preformed particle [29]. This approach can follow two primary routes by forming an MIP film on various substrates using spin-coating or dip-coating techniques [19,30,31]. The final step removes the stamp and template molecules, exposing binding sites on the MIP film surface. Alternatively, the approach of water-in-oil emulsion polymerisation generates core–shell particles, wherein a core (frequently silica particles) is used for stability and coated with an MIP shell using emulsion polymerisation [19]. Core–shell MIPs are advantageous over bulk MIPs in that all the binding sites are uniformly distributed near the surface for complete template removal without leakage and provide an improved rebinding of the target molecule along with enhanced mass-transfer efficiency, thus avoiding losses resulting from mechanical crushing and sieving, and hence, they are highly suitable for assays of specific targets [32]. In sum, core–shell MIPs ensure fast access to binding sites and are easy to regenerate, making them suitable for continuous or repetitive EC removal processes in fermented alcoholic beverage applications. On the other hand, they involve more complex synthesis because they require additional steps and precise control to ensure that binding sites are exposed properly, consequently lowering the binding capacity for binding large amounts of target molecules [25]. Han et al. [33] engineered two types of core–shell nanospheres as fluorescent probes using biomass carbon dots synthesised from watermelon peel, achieving a high-fluorescence quantum yield of 22.8% at a reduced cost. These probes, prepared via bulk polymerisation and sol–gel approaches, enable rapid EC detection in fermented alcoholic beverages with high sensitivity and precision and excellent reusability. Guo et al. [34] used EC as the template molecule and β-cyclodextrin derivatives as functional monomers. An EC molecularly imprinted sensor was developed through surface modification using MIT. The sensor successfully detected EC in Huangjiu with results comparable to those obtained via gas chromatography–mass spectrometry (GC-MS), demonstrating its reliability and potential for food and alcoholic beverage safety applications. Guo et al. [35] used the Diels–Alder (DA) reaction in the synthesis of MIPs through the reversible chemical interaction of specific structures of participating molecules in the system. Thus, the obtained new MIP is thermally switchable, possessing intelligent molecular recognition ability with thermal reversibility for EC adsorption. The performed absorption experiments prove that the obtained materials have strong specific absorption, and even after five recycling cycles, the recovery rate was maintained up to 88%. Zao et al. [36] developed a disposable electrochemical biomimetic sensor for the rapid, selective detection of EC in fermented alcoholic beverages, eliminating the need for complex sample preparation. By modifying a screen-printed carbon electrode with reduced graphene oxide and electropolymerizing o-aminophenol in the presence of EC as a template, the sensor achieved a wide linear detection range (100–1300 nM) with a low detection limit of 37 nM and rapid detection time (under 5 min). The development of sensors is simple; therefore, they are cheap, sensitive, and also chemically and mechanically robust.

Nano-MIPs offer an advanced solution in the miniaturisation of traditional MIPs to the nanoscale size (>100 nm), which allows for improved accessibility and binding efficiency for target analytes. Their surface-to-volume ratio raises the exposure of recognition sites,

allowing quick binding kinetics and great selectivity, which are critical for detecting trace levels of contaminants in fermented alcoholic beverages. The stability, sensitivity, and scope of application are influenced by each of these approaches. Nonetheless, nano-MIPs have some disadvantages related to the complexity of synthesis, which needs controlled polymerisation and may lead to inexpensive production and obstacles when scaling up. Such agglomeration during preparation may reduce the active surface area, and their reuse often results in the deterioration of the imprinted structure; hence, reusability is limited. In addition, maintaining the stability of such binding sites on these colloidal-sized particles is also highly questionable in conditions with variable pH and temperature, to which they will be exposed during any practical field application [37]. Wu et al. [38] reported an innovative nanozyme with a metal–organic framework and molecularly imprinted polymers with an EC-specific imprinted cavity, Co@MOF-MIP, exhibiting high peroxidase-like activity and blue fluorescence to enable onsite trimodal colorimetric, fluorescent, and photothermal detection of EC residues. The use of a trimodal detection system enhances the accuracy and depth of the analysis by way of Boolean-logic-based operations, enabling fast intelligent decision-making. Moreover, this nanozyme integrated with MIP provides a flexible and universal platform for point-of-care contaminant detection and may have possible smart monitoring applications in food safety.

4. Characterisation and Performance of Molecularly Imprinted Polymers for Ethyl Carbamate Removal

The preserved structure of the MIP cavity after template removal is thought to be critical, warranting thorough characterisation. The template-extracted cavity is indirectly assessed by examining the binding selectivity of MIPs with a non-imprinted polymer (NIP), prepared under the same conditions without the template, used for comparison to highlight the effects of imprinting [17,39]. Several techniques are used for characterising the chemical, morphological, and physicochemical (thermal adsorption, functional binding site) properties of MIPs, as shown in Figure 4.

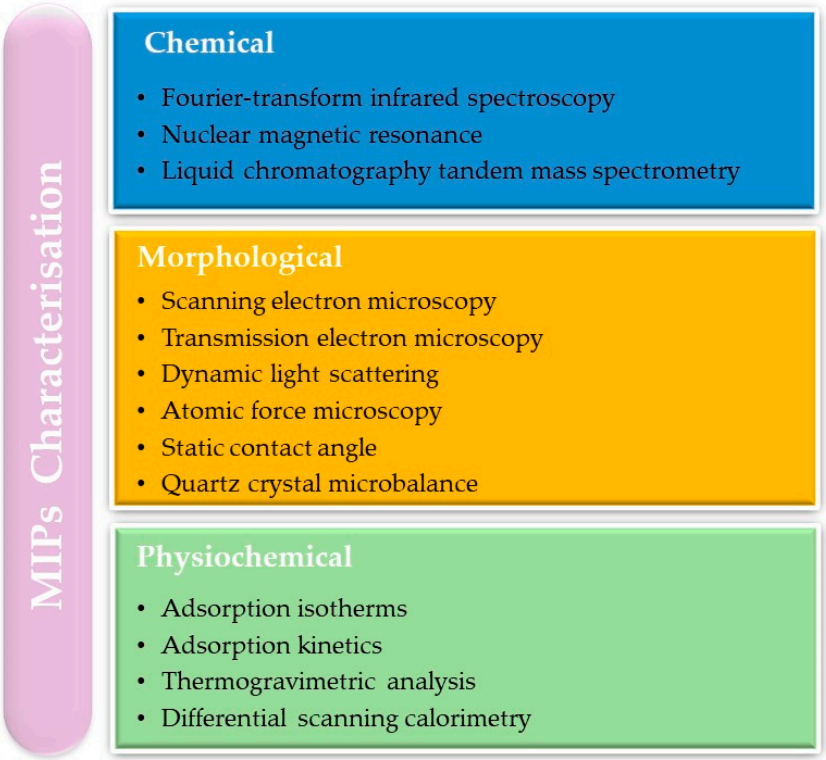


Figure 4. The most common techniques used for molecularly imprinted polymer characterisation.

Chemical characterisation techniques, such as Fourier-transform infrared spectroscopy (FTIR) and nuclear magnetic resonance (NMR, ^{1}H, and ^{13}C), are employed to analyse the chemical structure of MIPs. FTIR recognises individual functional groups of monomers, cross-linkers, and templates and investigates their interactions during MIP formation by examining specific absorption bands. FTIR also confirms the effective removal of the template molecule, showing access to an imprinted cavity upon changes within characteristic peaks in the forms of shifting, reduction intensity, and even disappearance of peaks. Likewise, FTIR can indicate secondary interactions, namely hydrogen bonding or van der Waals forces, occurring during the rebinding of the template [40]. The successful chemical transformations and structural incorporation during the synthesis of azide covalent organic frameworks $(COFs)_{(azide)}$-based materials were further confirmed by Meng et al. [41] using FTIR. Absorption of the azide peak at 2093 cm^{-1} and persistence of stretching bands due to C=O and C=N at 1590 cm^{-1} showed that post-modification by the copper-catalysed azide-alkyne cycloaddition reaction was successful. In addition, the characteristic peaks at 1731 cm^{-1} and 1257 cm^{-1} verified the presence of ester and carboxyl groups from ethylene glycol dimethacrylate and methacrylic acid, respectively, indicating the successful encapsulation of $COFs_{(azide)}$ within the core–shell nanomaterial structure to be used for capturing urea while eliminating EC from fermented alcoholic beverages.

Complementary insights into the MIP structure can be derived by NMR in solid-state and solution-state formats. In the solution state, NMR proves monomer–template interactions during pre-polymerisation complex formation by changes in chemical shift and coupling constants. Solid-state NMR can further explain the complete polymer structure, distinguishing between template-imprinted sites and cross-linked regions. Both techniques are also applied for template removal confirmation by comparing spectral data, and the mobility of the polymer chains near the imprinted sites can be evaluated by NMR relaxation measurements, thus offering a more detailed view of binding mechanisms. The integration of these techniques makes comprehensive characterisation possible, which is necessary to optimise functionality and specificity in MIPs [34,40,42,43]. Guo et al. [34] used the integration of FTIR and ^{13}C-NMR to confirm the structural incorporation and chemical transformations through the synthesis of an EC molecularly imprinted sensor (EC-MIS) using MIP surface modification. Guo et al. [35] confirmed the success of the DA reaction in DA-MIP by ^{13}C NMR. Key observations comprised the emergence of a signal at ~90 ppm, attributed to C8, the broadening of the carbonyl group peaks (~33.0 ppm), and the disappearance of furan ring signals (~110.4 ppm and ~141.1 ppm). Moreover, novel peaks appearing at 140.0 ppm for the C9/C10 carbon skeleton and 169.6 ppm for carbonyl groups indicated the DA bond and involvement of maleimide, thus confirming that the reaction occurred.

Techniques for morphological characterisation are vital for understanding and refining the surface and physical properties of MIPs. Scanning electron microscopy (SEM) and transmission electron microscopy (TEM) can be applied to evaluate surface morphology and particle size, providing vital details on the homogeneity and porosity of MIPs, which have a direct bearing on analyte diffusion and binding site accessibility. TEM can provide nanostructural details of thin films and surface-coated MIPs, including core–shell homogeneity and layer thickness [44]. Particle size analysis, usually carried out by laser diffraction or dynamic light scattering (DLS), provides quantitative data about particle size distribution and dispersion stability. In combination with BET analysis, these techniques characterise the surface area (m^2/g), pore volume (cm^3/g), and pore size distribution, thus providing a full understanding of the physical framework of MIPs. BET usually shows higher surface areas in MIPs compared to NIPs due to the creation of template-induced cavities [43]. For surface-deposited MIPs (e.g., films, membranes, sensor layers), atomic force

microscopy (AFM) provides high-resolution topographical maps, quantifying roughness parameters that influence binding performance. Insights into the wettability and chemical functionality of MIP surfaces can be obtained by static contact angle (SCA) measurements, which correlate surface hydrophobicity or hydrophilicity to functional monomer–template interactions. X-ray photoelectron spectroscopy (XPS), conducted for the confirmation of template removal, also provides information related to changes in elemental composition and the chemical state of the polymer matrix, often detecting residual template or functional group changes post-synthesis. To confirm the preliminary data obtained by FTIR, Han et al. [45] used XPS analysis to detect a peak at 288.8 eV in the C 1 s region, confirming that the Schiff base reaction had taken place between the main amine and aldehyde groups and consequently demonstrating that carbazole-based COFs were successfully synthesised. In the meantime, quartz crystal microbalance (QCM) offers real-time, label-free monitoring of the binding and unbinding events of target analytes and is thus of particular use in the study of MIP selectivity and affinity under different conditions. Further techniques such as ellipsometry are also applied to measure the thin film thickness and optical properties, which complement the morphological characterisation of MIPs in detail [17,35,39,43].

The quantification of the binding affinity and site distribution can be measured through adsorption isotherm models (e.g., Langmuir, Freundlich, Jovanovic, Scatchard, Langmuir–Freundlich), demonstrating the efficiency of MIPs in the selective detection of ECs from similar molecules. Monolayer adsorption on a surface with homogenous binding sites is proved by the Langmuir isotherm model, which admits homogeneous adsorption on a surface. The Langmuir isotherm model assumes that sorption occurs at particular uniform sites on the adsorbent; if a site is already occupied by the template molecule, more adsorption at that precise site is not feasible. An empirical formula assuming heterogeneous surface energy is the Freundlich isotherm model. The intercept of the linearised Freundlich plot, known as the heterogeneity index (m), indicates the surface's binding site heterogeneity, where a value of m close to 1 suggests homogeneous sites and a value near 0 indicates heterogeneous sites. Models like the Scatchard and Langmuir–Freundlich isotherms integrate features of these basic isotherms for further precision in describing MIP binding dynamics [17,45,46]. Adsorption kinetics frequently follow pseudo-second-order models, revealing specificity in the interaction between the EC and MIP binding sites, with the interaction being controlled by chemisorption. This model indicates that MIPs designed for EC have quick binding rates, particularly when surface-imprinted polymers are applied to improve accessibility and decrease diffusion restrictions in complex matrices [35,47,48]. According to Wu et al. [49], a pseudo-second-order kinetic model could accurately depict the adsorption reaction of MIPs towards EC. The correlation coefficient (R^2) value derived from the fitting curve (t/Qt vs. t) was 0.9991, and the Qe value derived from the linear regression model's slope was 3.91 mg/g, which was in good agreement with the experimental Qe value of 3.84 mg/g. As a result, chemical adsorption mechanisms that involve electron sharing between MIPs and EC regulate the adsorption process.

Thermogravimetric analysis (TGA) and differential scanning calorimetry (DSC), which are thermal characterisation techniques, are utilised to evaluate the thermal degradation pattern of MIPs in comparison to their NIPs. These techniques provide specific perceptions concerning the temperature range for the safe application of MIPs. TGA is of special importance in the optimisation of synthesis protocols due to the identification of residual solvents, unreacted monomers, or cross-linkers. In addition, TGA is performed to assess the thermal stability of MIPs concerning NIPs and to confirm the complete removal of templates, hence the efficiency of washing cycles [17]. Guo et al. [35], using TGA and DSG, observed different thermal properties of DA-MIPs and rDA (retro DA)-MIPs in terms of EC adsorption. No significant difference in thermal stability between MIPs and DA-MIPs was observed using

TCA curves. Both showed a total weight loss of 19–23% up to 600 °C, suggesting suitable thermal properties. DSC of DA-MIPs displayed an endothermic peak at ~130 °C, attributed to the fracture of DA adduct bonds, missing in MIPs and rDA-MIPs, which assured the presence of DA bonds in DA-MIPs. Thermodynamic studies on the adsorption of EC onto MIPs generally indicate exothermic and enthalpy-driven processes, which means that the optimal binding occurs under moderate-to-low temperatures. MIPs for EC are stable in the pH range relevant to alcoholic beverages, i.e., pH 3–4, and they maintain selective binding performance without degradation at moderate ethanol concentrations of up to 40% v/v, which is an indispensable requirement for stability in spirits and wines and generally in alcohol-rich matrices. Such properties further underline the suitability of MIPs for the selective removal of EC from different types of fermented alcoholic beverages, offering various beverage compositions in terms of robustness and effectiveness.

5. Molecularly Imprinted Polymers for Ethyl Carbamate Removal from Fermented Alcoholic Beverages

Recent studies have explored approaches to selectively remove, either indirectly (e.g., inhibiting the urea formation) or directly, EC from fermented alcoholic beverages without altering sensory properties (e.g., aroma, taste, and colour), which are essential to the product's character and market value. Integrating MIPs into beverage production and processing enable the extraction of EC and its precursors, thereby reducing both its formation and concentration. Practical applications, such as incorporating MIPs into filtration systems or solid-phase extraction (SPE) processes, highlight effective strategies for lowering EC levels in fermented alcoholic beverages, as shown in Table 2 [33,50,51]. So far, relatively few publications have discussed the binding or recognition capabilities of MIPs concerning EC, as well as its precursors.

Regarding indirect EC removal from fermented alcoholic beverages, urea is one of the most prominent and well-studied precursors in EC production. In yeast cells, enzymatic hydrolysis of arginine generates nearly 90% of EC from urea, indicating that reducing urea levels in fermented alcoholic beverages could significantly decrease the EC content. In this sense, Meng et al. [41] developed an azide COF-embedded MIP ($COFs_{(azide)}$@MIPs) platform for urea adsorption and indirect EC removal from Huangjiu. The platform's viability was demonstrated through the spiking recovery of Huangjiu samples, with recovery rates ranging from 88% to 109%, as shown in Table 2. In addition, the processing model attained a 39% reduction in EC levels, demonstrating the potential for addressing health concerns linked to fermented alcoholic beverages due to efficiently capturing and eliminating beverage hazards. Moreover, Meng et al. [52] developed a $COFs_{(azide)}$ framework conjugated with bionic antibody microspheres, namely $COFs_{(azide)}$@BAs, which precisely adsorbed urea, consequently reducing the EC levels in Huangjiu via indirect control. The spiked recoveries of Huangjiu samples varied from 85% to 110%, with a relative standard deviation (RSD) lower than 2.12%. In the simulated system, the $COFs_{(azide)}$@BAs displayed the effective inhibition of EC, since the initial EC concentration was reduced from 103 mg/L to 75 mg/L, representing an inhibition rate of 27%.

Table 2. Indirect and direct approaches to remove ethyl carbamate from fermented alcoholic beverages.

Matrix	MIP or Modified MIP	Main Results	Ref
Indirect approach			
Huangjiu	COFs(azide)@MIPs	LOD = 16 ng/L Linearity range: 0–5 μg/L Recovery: 88–109% The processing model attained a 39% reduction in EC levels	[41]
Huangjiu	COFs(azide)@BAs	LOD = 13 ng/L Linearity range: 0.05–5 μg/L Recovery: 85–110% The initial EC concentration was reduced from 103 mg/L to 75 mg/L, representing an inhibition rate of 27%	[52]
Direct approach			
Rice wine, fruit brandy	MIPs–SERS	Recovery: 84–102% MIPs-SERS is suitable for EC quantification and can quickly and precisely remove EC from rice wine and fruit brandy	[49]
Liquor	Fe_3O_4@COFs	Recovery = 87–116% Fe_3O_4@COFs demonstrated excellent stability and exceptional performance in removing EC from liquor	[48]
Huangjiu	MIPs based on β-cyclodextrin derivatives	LOD = 5.86 μg/L EC-MIS proved to be suitable for EC detection and, consequently, EC removal	[34]
Baijiu, Huangjiu, plum wine	$COFs_{(carbazole)}$@MIPs	LOD = 607 ng/L Recovery: 85–109% MIPs on carbazole-based COFs were suitable to selectively quantify EC in a diversity of fermented alcoholic beverages	[45]
Liquors	CDs@MIPs	LOD = 0.57–0.94 μg/L Recovery = 84–144% CDs@MIPs proved to be highly efficient in the recognition of trace EC in real samples	[33]
Baijiu, Huangjiu	GFPNs@PMIPs	LOD = 0.82–1.65 μg/L Recovery = 84–107% GFPNs@PMIPs demonstrated specific EC recognition and removal via the charge-transfer effect	[51]
Distilled spirits	MIP/rGO/SPCE	LOD = 37 nM Recovery = 99–100% MIP/rGO/SPCE provides a novel opportunity for the real-time detection of EC without sample pretreatment	[36]

Abbreviations: CDs@MIPs—biomass carbon dots embedded in molecularly imprinted polymers; EC—ethyl carbamate; Fe_3O_4@COFs—magnetic iron oxide@covalent organic frameworks; GFPNs@PMIPs—genipin-H-Phe-Phe-OH nanoparticles@peptide-based molecularly imprinted polymers; LOD—limit of detection; MIP/rGO/SPCE—molecularly imprinted polymers/reduced graphene oxide/screen-printed carbon composite electrode; MIPs–SERS—molecularly imprinted polymers and surface-enhanced Raman spectroscopy.

Regarding direct EC removal, Baggiani et al. [21] used acrylamide and methacrylic acid as functional monomers to develop two types of MIPs to recognise and capture EC. In this study, chloroform was also used as a porogen to enhance polymer selectivity, and the results highlighted that the carbamate group was critical for recognition; the shape and size of the substituents further modulated the selectivity in favour of analogues slightly larger than the template. As a result, methacrylic acid became the preferred functional monomer in later studies on MIP synthesis via bulk polymerisation. With their low cost and robust structures, MIPs see growing use as recognition elements in sensors, and a major trend in current sensor research involves integrating MIPs' selective recognition abilities with the sensitivity of electrochemical detection. Yan et al. [48] proposed an efficient approach for eliminating EC from liquors using a magnetic mesoporous adsorbent (Fe_3O_4@COFs) with great adsorption effectiveness and quick action. The adsorption process was monitored by gas chromatography–tandem mass spectrometry (GC-MS/MS), and it was found that the Fe_3O_4@COFs adsorbent followed a pseudo-second-order kinetic model and attained elevated recovery rates (87–116%) and a lower RSD < 5.8%. The Fe_3O_4@COFs adsorbent exhibited stability and a robust approach for EC removal, indicating its future pertinency for pretreatment in liquors. Han et al. [51] exploited a peptide-based MIP (PMIP) platform, using genipin-H-Phe-Phe-OH nanoparticles (GFPNs) as a fluorescent optosensing core for EC detection. The obtained GFPNs@PMIPs showed a dual red–blue fluorescence with a lower limit of detection (LOD, 0.82–1.65 μg/L) and high accuracy with spiked recoveries rates ranging from 84% to 107%. Moreover, the platform was coupled with a smartphone application for real-time and on-site detection, enabling visual confirmation utilising red (R) value changes upon EC detection. This approach illustrates a new portable method for monitoring of EC in fermented alcoholic beverages. Studies investigating MIP performance for the removal of EC in fermented alcoholic beverages (wines, liquor, brandies) reveal that MIPs generally retain their selective binding in alcoholic beverages. Moreover, MIPs are used to selectively remove contaminants (e.g., ochratoxin A, bisphenol A, volatile phenols) from fermented alcoholic beverages [53–57].

6. Comparison of MIT with Other Strategies to Reduce Ethyl Carbamate in Fermented Alcoholic Beverages

Over recent decades, several traditional strategies have been implemented to mitigate EC from fermented alcoholic beverages, such as the metabolic engineering modification of yeast (e.g., enhancing the expressions of DUR3), enzymatic methods (e.g., adding acid urease), chemical (e.g., copper catalysts), and physical (e.g., charcoal filtration, low temperature, deoxygenated conditions, de-stoning process) [58], as shown in Figure 5.

Wu et al. [59] developed a metabolically engineered yeast strain, $N85^{DUR1,2/DUR3}$-c, to decrease the level of EC in Chinese rice wine. Overexpression of the DUR3 gene was mediated by a CRISPR/Cas9 system and resulted in 92% and 59% reductions in urea and EC concentrations, respectively, compared to the original strain. The engineered strain showed genetic stability and did not affect yeast growth or fermentation performance, making it a promising candidate for application in rice wine production with reduced EC levels. Han et al. [60] genetically engineered *Saccharomyces cerevisiae* strains to destroy EC using the urethanase gene (UreA) from Micrococcus species, which converts EC into ethanol and ammonia. Surface-displayed urethanase (EBY100/Aga2-UreA) showed the greatest degradation efficiency, eliminating 476 mg/L EC in 84 h, a 31% enhancement over extracellular UreA expression. Under pH 5.0 conditions in the bioreactor, this strain degraded an additional 519 mg/L EC, thus demonstrating the effectiveness of enzyme surface display for reducing toxic compounds during fermentation processes. Dong et al. [61] isolated a novel EC hydrolase (ECH) from *Acinetobacter calcoaceticus* with a high specificity of 68.31 U/mg

and excellent tolerance to extreme conditions (e.g., ethanol, retaining up to 40% activity at 60% ethanol within 1 h) and elevated salt concentrations. The immobilised ECH decreased 71.6 μg/L of the EC in the liquor in 12 h with insignificant influence on flavour molecules, suggesting this may hold industrial applications for fermented alcoholic beverage improvement. However, all these approaches usually have disadvantages, e.g., low scalability (e.g., metabolic engineering), potential off-flavours or toxicity (e.g., copper catalysts), elevated operational costs (e.g., enzymatic treatments), and low efficacy under industrial fermentation conditions (e.g., physical methods) [58]. MIPs have higher initial costs and face regulatory challenges, but in several key respects, this approach outperforms traditional strategies for EC removal in beverage production due to their superior performance in terms of selectivity (yielding up to 84% efficiency in fermented alcoholic beverages) and their excellent cyclic stability and reusability. In addition, preservation of beverage quality is ensured by the minimum removal of desirable flavour compounds, and the method is cost-effective over the long term, even considering the higher initial synthesis costs. In contrast, most traditional strategies, such as enzymatic degradation or physical adsorption, usually lack specificity; they often require more frequent material replacement or regeneration and can also remove other components inadvertently, compromising beverage quality. From an economic perspective, the feasibility of applying MIP technology will be measured in terms of production costs, scalability, and efficiency relative to traditional mitigation strategies. While MIPs have the potential to offer high selectivity and recyclability and potentially lower waste product generation, preparation and processing may be more costly. However, if MIPs have enhanced contaminant removal efficiency with reduced replacement frequency and total operating cost, they could prove to be a low-cost alternative in the long run. A sound cost–benefit analysis would be essential to ascertain their economic viability compared to traditional strategies (e.g., activated carbon filtration, ion exchange) [13,61,62].

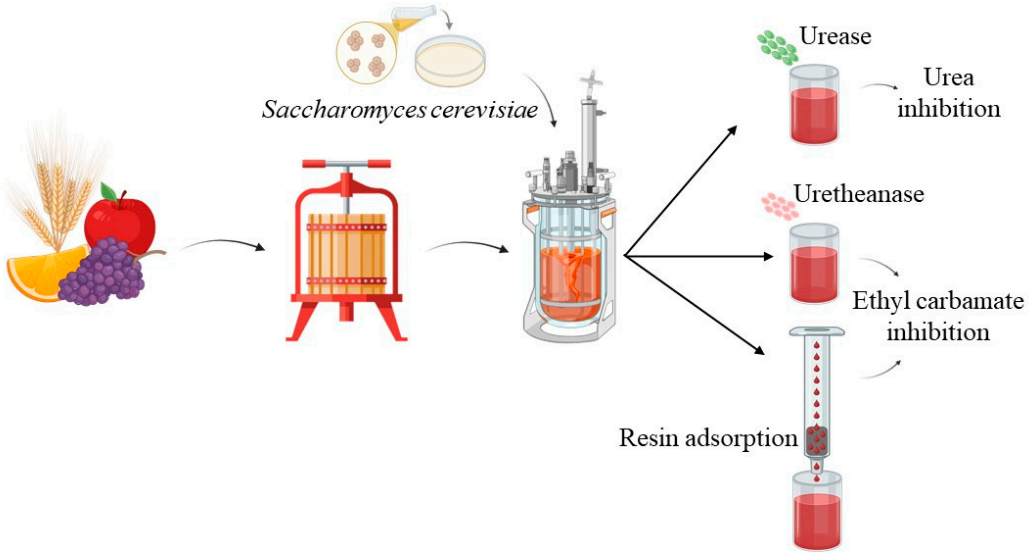


Figure 5. Traditional strategies to mitigate ethyl carbamate from fermented alcoholic beverages.

7. Challenges and Future Directions

The applicability of MIPs to remove or inhibit EC in fermented alcoholic beverages represents a suitable approach to food safety. However, several challenges should be considered, such as reproducibility, cost, process scalability, quality control, and material handling, before scaling up the production of MIPs for EC removal. For enormous batch runs of reliable quality and performance, the synthesis parameters of temperature, mixing durations, and monomer–template ratios might be crucial. It is difficult to guarantee

consistency in binding capacity and selectivity for EC on a larger scale, since even little adjustments to these parameters might have a significant impact on the binding characteristics of this polymer. The initial investment in the manufacture of MIPs can be very high, especially due to the special materials required for synthesis and controlled environments for optimal polymerisation. In addition, costs related to optimisation and validation of production processes are extremely high, especially for small- and medium-sized producers that may not have many resources. Most approaches to MIP synthesis effective at a laboratory scale will not translate industrially, since polymerisation techniques have disadvantages; poor mixing and heat transfer can occur, which could compromise quality and properties in large volumes of MIPs. Ensuring quality control in large-scale production is vital for maintaining the specifications that MIPs must meet for EC binding. Rigorous testing and characterisation will add to the complexity and expense of such a production process. Large-scale processing and handling could also present a problem of material stability and degradation, especially if the products or starting material consists of labile compounds [44,50,63]. Organic solvents and chemicals used during synthesis may often pose environmental hazards unless subjected to proper management. The use of fewer toxic solvents and some alternative methods of polymerisation are some of the green chemistry principles that minimise environmental impacts during MIP production. The residuals of MIPs and the remaining chemicals used for their synthesis are difficult to dispose of. If MIPs are prepared for single use, they can be one of the causes of waste generation. For this purpose, sustainable disposal techniques need to be developed. This issue can be overcome by research on biodegradable alternatives or any recycling methods for MIPs. The life cycle assessment of MIPs will help to show the environmental impacts from production to disposal. A holistic view can point out areas that need improvement in the production process for sustainability [64].

The introduction of MIPs into the production of fermented alcoholic beverages is subject to food safety legislations, which vary by region. These usually require a full safety assessment by relevant regulatory bodies, such as the FDA in the United States or EFSA in Europe, to confirm that MIPs will not leach harmful substances into fermented beverages or otherwise affect the quality of the beverage. All new materials coming into contact with food, including MIPs, will need to be rigorously evaluated and approved regarding their safety, efficacy, and interaction with food components. This can include detailed studies on the migration of chemical compounds, their eventual toxicity, and long-term effects on consumers. Moreover, if in direct contact with beverages or food products, MIP materials must comply with Regulation (EC) No 1935/2004 [65,66]. The regulation lays down general safety and inertness principles for all food-contacting materials so that they do not transfer constituents to food at levels harmful to human health or change food composition, taste, and odour in an unacceptable way [65]. On the other hand, if the MIP radically alters the nature or makeup of the food product, it would be within the scope of Novel Food Regulation (EU) 2015/2283 and would have to be authorised. The regulation provides a regulatory framework for placing novel foods on the European Union market to grant a high level of protection for human health and the interests of consumers [67]. The problems a winery might experience concern labelling requirements and conformance with local and international standards. Extra administrative work is required regarding MIP-treated beverages to meet their criteria for marketing and consumer information without compromising safety or environmental integrity.

Future research on MIPs for applications in fermented alcoholic beverage production and other industries will likely involve the following areas of high promise: advanced MIP materials, hybrid MIP nanocomposites, artificial intelligence (AI) in MIP design, sustainability in MIP production, and long-term stability and reusability. Therefore, inves-

tigating novel monomers, cross-linkers, and templates can lead to MIPs with improved selectivity and binding capacities. The development of hybrid materials, combining MIPs with nanoparticles or other functional materials, will allow for the improvement of mechanical stability, surface area, and binding kinetics. By incorporating machine learning and computational modelling into the design process, MIP selectivity and synthesis efficiency may be significantly improved. AI will enable synthesis condition optimisation, template–monomer interaction prediction, and the identification of the optimal polymer topologies to target a particular analyte. Sustainability in synthesis will reduce the environmental impact of MIP manufacturing, including the development of more environmentally friendly solvents or waste-derived feedstocks. Important information for consumer safety will be obtained from further studies on the long-term stability, regeneration processes, and cost-effectiveness of MIPs in diverse fermented beverage matrices. Investigating these fields will help create more effective, economical, and ecologically friendly MIP technologies that improve performance and selectivity in applications like winemaking and others [50].

8. Conclusions

MIPs provide a direct or indirect efficient and selective strategy for removing EC from fermented alcoholic beverages. Compared to traditional adsorbents, their design enables increased binding capabilities by specifically recognising EC. Studies show that MIPs may sustain binding performance across several cycles, which increases their cost-effectiveness and makes them a feasible option for long-term fermented alcoholic beverage processing applications. Their selective properties contribute to reducing the possibility of binding to non-target components; consequently, MIPs are indispensable in solving EC problems in fermented alcoholic beverages without changing their sensory properties (e.g., taste, colour, odour). The continued development of MIP technology increases their potential for commercial applications, namely, the integration of MIPs into the production of fermented alcoholic beverages without sacrificing quality with practical selection as food safety regulations constrict and consumer consciousness of pollutants grows. Scalability of production and continuous research towards the improvement of MIP designs support their practicality in large-scale beverage production, hence positioning them as a prime instrument in pioneering production processes. Methacrylic-acid-based polymers, polystyrene, polyacrylamide, silica-based polymers, and hybrid organic–inorganic materials exhibit promising MIP matrices. Most MIPs are based on methacrylic acid due to the high hydrogen bonding between methacrylic acid and EC, which enhances the selectivity and adsorption efficiency. Silica-based MIPs have excellent thermal and chemical stability and, hence, may find applications at the industrial level. Hybrid materials with inorganic elements have superior mechanical strength and reusability; hence, they are more suitable for large-scale applications in beverage processing. These latest developments ensure that MIPs are among the modern approaches for the removal of ECs in fermented alcoholic beverages.

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References

1. Rowe, S.; Alexander, N.; Kretser, A.; Steele, R.; Kretsch, M.; Applebaum, R.; Clydesdale, F.; Cummins, D.; Hentges, E.; Navia, J.; et al. Principles for Building Public-Private Partnerships to Benefit Food Safety, Nutrition, and Health Research. *Nutr. Rev.* **2013**, *71*, 682–691. [CrossRef] [PubMed]
2. Oladunjoye, A.O.; Awani-Aguma, E.U. Chapter 7 Foodborne Illnesses: Prevention and Control. In *Food Safety and Toxicology*; Ijabadeniyi, O., Olagunju, O.F., Eds.; De Gruyter: Berlin, Germany, 2023; pp. 149–174.
3. Onyeaka, H.; Ghosh, S.; Obileke, K.; Miri, T.; Odeyemi, O.A.; Nwaiwu, O.; Tamasiga, P. Preventing Chemical Contaminants in Food: Challenges and Prospects for Safe and Sustainable Food Production. *Food Control* **2024**, *155*, 110040. [CrossRef]
4. Abt, E.; Incorvati, V.; Robin, L.P.; Redan, B.W. Occurrence of Ethyl Carbamate in Foods and Beverages: Review of the Formation Mechanisms, Advances in Analytical Methods, and Mitigation Strategies. *J. Food Prot.* **2021**, *84*, 2195–2212. [CrossRef] [PubMed]
5. Jia, W.; Di, C.; Zhang, R.; Shi, L. Ethyl Carbamate Regulate Esters Degradation by Activating Hydrolysis during Baijiu Ripening. *Food Res. Int.* **2022**, *156*, 111157. [CrossRef]
6. Jung, J.-Y.; Kang, M.-J.; Hwang, H.-S.; Baek, K.-R.; Seo, S.-O. Reduction of Ethyl Carbamate in an Alcoholic Beverage by CRISPR/Cas9-Based Genome Editing of the Wild Yeast. *Foods* **2022**, *12*, 102. [CrossRef]
7. Han, B.; Zhang, S.; Chen, L.; Ren, X.; Li, D. Distribution, Generation, and Control of Ethyl Carbamate in Baijiu: A Review. *Food Control* **2025**, *168*, 110951. [CrossRef]
8. Xia, Q.; Yang, C.; Wu, C.; Zhou, R.; Li, Y. Quantitative Strategies for Detecting Different Levels of Ethyl Carbamate (EC) in Various Fermented Food Matrices: An Overview. *Food Control* **2018**, *84*, 499–512. [CrossRef]
9. Shalamitskiy, M.Y.; Tanashchuk, T.N.; Cherviak, S.N.; Vasyagin, E.A.; Ravin, N.V.; Mardanov, A.V. Ethyl Carbamate in Fermented Food Products: Sources of Appearance, Hazards and Methods for Reducing Its Content. *Foods* **2023**, *12*, 3816. [CrossRef]
10. Tian, S.; Zeng, W.; Zhou, J.; Du, G. Correlation between the Microbial Community and Ethyl Carbamate Generated during Huzhou Rice Wine Fermentation. *Food Res. Int.* **2022**, *154*, 111001. [CrossRef]
11. European Union Commission Recommendation (EU) 2016/22 of 7 January 2016 on the Prevention and Reduction of Ethyl Carbamate Contamination in Stone Fruit Spirits and Stone Fruit Marc Spirits, Repealing Recommendation 2010/133/EU. Available online: https://eur-lex.europa.eu/eli/reco/2016/22/oj/eng (accessed on 13 February 2025).
12. Canada Food Inspection Agency. *Ethyl Carbamate in Fermented Soy Products and Cooking Wine–1 April 2022 to 31 March 2023*; Canada Food Inspection Agency: Calgary, Canada, 2023.
13. Chen, Y.; Zeng, W.; Fang, F.; Yu, S.; Zhou, J. Elimination of Ethyl Carbamate in Fermented Foods. *Food Biosci.* **2022**, *47*, 101725. [CrossRef]
14. Yan, X.; Almajidi, Y.Q.; Uinarni, H.; Bokov, D.O.; Mansouri, S.; Fenjan, M.N.; Saxena, A.; Zabibah, R.S.; Hamzah, H.F.; Oudah, S.K. Bio(Sensors) Based on Molecularly Imprinted Polymers and Silica Materials Used for Food Safety and Biomedical Analysis: Recent Trends and Future Prospects. *Talanta* **2024**, *276*, 126292. [CrossRef] [PubMed]
15. Ayerdurai, V.; Cieplak, M.; Kutner, W. Molecularly Imprinted Polymer-Based Electrochemical Sensors for Food Contaminants Determination. *TrAC Trends Anal. Chem.* **2023**, *158*, 116830. [CrossRef]
16. Geng, L.; Huang, J.; Fang, M.; Wang, H.; Liu, J.; Wang, G.; Hu, M.; Sun, J.; Guo, Y.; Sun, X. Recent Progress of the Research of Metal-Organic Frameworks-Molecularly Imprinted Polymers (MOFs-MIPs) in Food Safety Detection Field. *Food Chem.* **2024**, *458*, 140330. [CrossRef]
17. Mabrouk, M.; Hammad, S.F.; Abdella, A.A.; Mansour, F.R. Tips and Tricks for Successful Preparation of Molecularly Imprinted Polymers for Analytical Applications: A Critical Review. *Microchem. J.* **2023**, *193*, 109152. [CrossRef]
18. Mokhtari, P.; Ghaedi, M. Water Compatible Molecularly Imprinted Polymer for Controlled Release of Riboflavin as Drug Delivery System. *Eur. Polym. J.* **2019**, *118*, 614–618. [CrossRef]
19. Villa, C.C.; Sánchez, L.T.; Valencia, G.A.; Ahmed, S.; Gutiérrez, T.J. Molecularly Imprinted Polymers for Food Applications: A Review. *Trends Food Sci. Technol.* **2021**, *111*, 642–669. [CrossRef]
20. Włoch, M.; Datta, J. Chapter 2 Synthesis and Polymerisation Techniques of Molecularly Imprinted Polymers. In *Comprehensive Analytical Chemistry*; Elsevier: Amsterdam, The Netherlands, 2019; pp. 17–40.
21. Baggiani, C.; Anfossi, L.; Baravalle, P.; Giovannoli, C.; Tozzi, C. Selectivity Features of Molecularly Imprinted Polymers Recognising the Carbamate Group. *Anal. Chim. Acta* **2005**, *531*, 199–207. [CrossRef]
22. Wackerlig, J.; Schirhagl, R. Applications of Molecularly Imprinted Polymer Nanoparticles and Their Advances toward Industrial Use: A Review. *Anal. Chem.* **2016**, *88*, 250–261. [CrossRef]
23. Lovell, P.A.; Schork, F.J. Fundamentals of Emulsion Polymerization. *Biomacromolecules* **2020**, *21*, 4396–4441. [CrossRef]
24. Sun, Y.; Zhang, Y.; Ju, Z.; Niu, L.; Gong, Z.; Xu, Z. Molecularly Imprinted Polymers Fabricated by Pickering Emulsion Polymerization for the Selective Adsorption and Separation of Quercetin from Spina Gleditsiae. *New J. Chem.* **2019**, *43*, 14747–14755. [CrossRef]
25. Dong, C.; Shi, H.; Han, Y.; Yang, Y.; Wang, R.; Men, J. Molecularly Imprinted Polymers by the Surface Imprinting Technique. *Eur. Polym. J.* **2021**, *145*, 110231. [CrossRef]

26. Zheng, W.; Yao, M.; Leng, Y.; Yu, K.; Xiao, X.; Huang, H.; Yu, X.; Ma, Y.; Hou, C. Direct Detection of Ethyl Carbamate in Baijiu by Molecularly Imprinted Electrochemical Sensors Based on Perovskite and Graphene Oxide. *Food Chem. X* **2024**, *23*, 101752. [CrossRef]
27. Dai, C.; Zhou, X.; Zhang, Y.; Liu, S.; Zhang, J. Synthesis by Precipitation Polymerization of Molecularly Imprinted Polymer for the Selective Extraction of Diclofenac from Water Samples. *J. Hazard. Mater.* **2011**, *198*, 175–181. [CrossRef] [PubMed]
28. Yang, H.; Liu, H.-B.; Tang, Z.-S.; Qiu, Z.-D.; Zhu, H.-X.; Song, Z.-X.; Jia, A.-L. Synthesis, Performance, and Application of Molecularly Imprinted Membranes: A Review. *J. Environ. Chem. Eng.* **2021**, *9*, 106352. [CrossRef]
29. Bayramoglu, G.; Arica, M.Y.; Liman, G.; Celikbicak, O.; Salih, B. Removal of Bisphenol A from Aqueous Medium Using Molecularly Surface Imprinted Microbeads. *Chemosphere* **2016**, *150*, 275–284. [CrossRef]
30. BelBruno, J.J. Molecularly Imprinted Polymers. *Chem. Rev.* **2019**, *119*, 94–119. [CrossRef]
31. Wang, S.; Zhang, L.; Zeng, J.; Hu, X.; Wang, X.; Yu, L.; Wang, D.; Cheng, L.; Ahmed, R.; Romanovski, V.; et al. Multi-Templates Molecularly Imprinted Polymers for Simultaneous Recognition of Multiple Targets: From Academy to Application. *TrAC Trends Anal. Chem.* **2023**, *166*, 117173. [CrossRef]
32. Soliman, S.S.; Mahmoud, A.M.; Elghobashy, M.R.; Zaazaa, H.E.; Sedik, G.A. Point-of-Care Electrochemical Sensor for Selective Determination of Date Rape Drug "Ketamine" Based on Core-Shell Molecularly Imprinted Polymer. *Talanta* **2023**, *254*, 124151. [CrossRef]
33. Han, L.; Zhu, P.; Liu, H.; Sun, B. Molecularly Imprinted Bulk and Solgel Optosensing Based on Biomass Carbon Dots Derived from Watermelon Peel for Detection of Ethyl Carbamate in Alcoholic Beverages. *Microchim. Acta* **2022**, *189*, 286. [CrossRef]
34. Guo, M.; Hu, Y.; Wang, L.; Brodelius, P.E.; Sun, L. A Facile Synthesis of Molecularly Imprinted Polymers and Their Properties as Electrochemical Sensors for Ethyl Carbamate Analysis. *RSC Adv.* **2018**, *8*, 39721–39730. [CrossRef]
35. Guo, M.; Zhang, X.; Zheng, Y.; Huang, D. Synthesis of Switchable Intelligent Molecularly Imprinted Polymers with Selective Adsorption of Ethyl Carbamate and Their Application in Electrochemical Sensor Analysis. *RSC Adv.* **2018**, *8*, 25636–25644. [CrossRef]
36. Zhao, X.; Zuo, J.; Qiu, S.; Hu, W.; Wang, Y.; Zhang, J. Reduced Graphene Oxide-Modified Screen-Printed Carbon (RGO-SPCE)-Based Disposable Electrochemical Sensor for Sensitive and Selective Determination of Ethyl Carbamate. *Food Anal. Methods* **2017**, *10*, 3329–3337. [CrossRef]
37. Mahmoudpour, M.; Torbati, M.; Mousavi, M.-M.; de la Guardia, M.; Ezzati Nazhad Dolatabadi, J. Nanomaterial-Based Molecularly Imprinted Polymers for Pesticides Detection: Recent Trends and Future Prospects. *TrAC Trends Anal. Chem.* **2020**, *129*, 115943. [CrossRef]
38. Wu, G.; Liu, S.; Du, C.; Huang, M.; Wu, Y.; Shen, Y. A Versatile Visual Molecular Imprinting-Driven Switchable Nanozyme Activity-Based Trimodal Assay and Logic Gate Circuits of Ethyl Carbamate. *Anal. Chem.* **2024**, *96*, 14706–14713. [CrossRef] [PubMed]
39. Poonia, K.; Raizada, P.; Singh, A.; Verma, N.; Ahamad, T.; Alshehri, S.M.; Khan, A.A.P.; Singh, P.; Hussain, C.M. Magnetic Molecularly Imprinted Polymer Photocatalysts: Synthesis, Applications and Future Perspective. *J. Ind. Eng. Chem.* **2022**, *113*, 1–14. [CrossRef]
40. Luo, Y. Innovative Methods of Synthesis and Characterization for Molecularly Imprinted Polymers. *Open J. Appl. Sci.* **2024**, *14*, 2559–2579. [CrossRef]
41. Meng, C.; Li, S.; Zhang, D.; Liu, H.; Sun, B. Conjugated Molecularly Imprinted Polymers Based on Covalent Organic Frameworks: Fluorescent Sensing Platform for Specific Capture of Urea and Elimination of Ethyl Carbamate. *Spectrochim. Acta A Mol. Biomol. Spectrosc.* **2024**, *316*, 124357. [CrossRef]
42. Hasanah, A.N.; Safitri, N.; Zulfa, A.; Neli, N.; Rahayu, D. Factors Affecting Preparation of Molecularly Imprinted Polymer and Methods on Finding Template-Monomer Interaction as the Key of Selective Properties of the Materials. *Molecules* **2021**, *26*, 5612. [CrossRef]
43. De Middeleer, G.; Dubruel, P.; De Saeger, S. Characterization of MIP and MIP Functionalized Surfaces: Current State-of-the-Art. *TrAC Trends Anal. Chem.* **2016**, *76*, 71–85. [CrossRef]
44. Wackerlig, J.; Lieberzeit, P.A. Molecularly Imprinted Polymer Nanoparticles in Chemical Sensing–Synthesis, Characterisation and Application. *Sens. Actuators B Chem.* **2015**, *207*, 144–157. [CrossRef]
45. Han, L.; Meng, C.; Zhang, D.; Liu, H.; Sun, B. Fabrication of a Fluorescence Probe via Molecularly Imprinted Polymers on Carbazole-Based Covalent Organic Frameworks for Optosensing of Ethyl Carbamate in Fermented Alcoholic Beverages. *Anal. Chim. Acta* **2022**, *1192*, 339381. [CrossRef]
46. García-Calzón, J.A.; Díaz-García, M.E. Characterization of Binding Sites in Molecularly Imprinted Polymers. *Sens. Actuators B Chem.* **2007**, *123*, 1180–1194. [CrossRef]
47. Murray, A.; Örmeci, B. Application of Molecularly Imprinted and Non-Imprinted Polymers for Removal of Emerging Contaminants in Water and Wastewater Treatment: A Review. *Environ. Sci. Pollut. Res.* **2012**, *19*, 3820–3830. [CrossRef] [PubMed]

48. Yang, S.; Wang, Y.; He, J.; Yang, R.; Ma, X.; Yuan, Y.; Yue, T.; Sheng, Q. Functionalized Magnetic Covalent Organic Framework Nanocomposites for High-efficiency Adsorption of Ethyl Carbamate from Liquor. *Food Front.* **2023**, *4*, 911–921. [CrossRef]
49. Wu, Z.; Xu, E.; Li, J.; Long, J.; Jiao, A.; Jin, Z. Highly Sensitive Determination of Ethyl Carbamate in Alcoholic Beverages by Surface-Enhanced Raman Spectroscopy Combined with a Molecular Imprinting Polymer. *RSC Adv.* **2016**, *6*, 109442–109452. [CrossRef]
50. Meng, C.; Liu, H.; Sun, B. Molecularly Imprinted Polymers: A New Solution for Controlling Ethyl Carbamate in Fermented Alcoholic Beverages. *Sep. Purif. Rev.* **2024**, *54*, 17–36. [CrossRef]
51. Han, L.; Zhu, X.; Zhang, D.; Liu, H.; Sun, B. Peptide-Based Molecularly Imprinted Polymer: A Visual and Digital Platform for Specific Recognition and Detection of Ethyl Carbamate. *ACS Sens.* **2023**, *8*, 694–703. [CrossRef]
52. Meng, C.; Chen, Y.; Zhang, D.; Liu, H.; Sun, B. Stable Light-Emitting Bionic Antibody-Conjugated Covalent Organic Frameworks for the Adsorption of Urea and Control of Ethyl Carbamate. *Sens. Actuators B Chem.* **2024**, *401*, 134917. [CrossRef]
53. Tsalbouris, A.; Kalogiouri, N.P.; Kabir, A.; Furton, K.G.; Samanidou, V.F. Bisphenol A Migration to Alcoholic and Non-Alcoholic Beverages—An Improved Molecular Imprinted Solid Phase Extraction Method Prior to Detection with HPLC-DAD. *Microchem. J.* **2021**, *162*, 105846. [CrossRef]
54. Liao, F.-Y.; Weng, J.-R.; Lin, Y.-C.; Feng, C.-H. Molecularly Imprinted Dispersive Micro Solid-Phase Extraction and Tandem Derivatization for the Determination of Histamine in Fermented Wines. *Anal. Bioanal. Chem.* **2024**, *416*, 945–957. [CrossRef]
55. Li, H.-Z.; Qian, H.-L.; Xu, S.-T.; Yang, C.; Yan, X.-P. Tuning the Planarity of Molecularly Imprinted Covalent Organic Frameworks for Selective Extraction of Ochratoxin A in Alcohol Samples. *Food Chem.* **2024**, *451*, 139427. [CrossRef] [PubMed]
56. Liu, Y.; Su, Z.; Wang, J.; Gong, Z.; Lyu, H.; Xie, Z. Molecularly Imprinted Polymer with Mixed-Mode Mechanism for Selective Extraction and on-Line Detection of Ochratoxin A in Beer Sample. *Microchem. J.* **2021**, *170*, 106696. [CrossRef]
57. Filipe-Ribeiro, L.; Cosme, F.; Nunes, F.M. New Molecularly Imprinted Polymers for Reducing Negative Volatile Phenols in Red Wine with Low Impact on Wine Colour. *Food Res. Int.* **2020**, *129*, 108855. [CrossRef]
58. Zhao, X.; Du, G.; Zou, H.; Fu, J.; Zhou, J.; Chen, J. Progress in Preventing the Accumulation of Ethyl Carbamate in Alcoholic Beverages. *Trends Food Sci. Technol.* **2013**, *32*, 97–107. [CrossRef]
59. Wu, D.; Xie, W.; Li, X.; Cai, G.; Lu, J.; Xie, G. Metabolic Engineering of Saccharomyces Cerevisiae Using the CRISPR/Cas9 System to Minimize Ethyl Carbamate Accumulation during Chinese Rice Wine Fermentation. *Appl. Microbiol. Biotechnol.* **2020**, *104*, 4435–4444. [CrossRef]
60. Han, K.; Lee, H.; Kang, T.-G.; Lee, J.; Kim, S.-K. Direct and Efficient Elimination of Ethyl Carbamate by Engineered Saccharomyces Cerevisiae Displaying Urethanase. *Food Control* **2022**, *142*, 109236. [CrossRef]
61. Dong, N.; Xue, S.; Guo, H.; Xiong, K.; Lin, X.; Liang, H.; Ji, C.; Huang, Z.; Zhang, S. Genetic Engineering Production of Ethyl Carbamate Hydrolase and Its Application in Degrading Ethyl Carbamate in Chinese Liquor. *Foods* **2022**, *11*, 937. [CrossRef]
62. Guo, X.-W.; Li, Y.-Z.; Guo, J.; Wang, Q.; Huang, S.-Y.; Chen, Y.-F.; Du, L.-P.; Xiao, D.-G. Reduced Production of Ethyl Carbamate for Wine Fermentation by Deleting CAR1 in Saccharomyces Cerevisiae. *J. Ind. Microbiol. Biotechnol.* **2016**, *43*, 671–679. [CrossRef]
63. Bagheri, A.R.; Aramesh, N.; Khan, A.A.; Gul, I.; Ghotekar, S.; Bilal, M. Molecularly Imprinted Polymers-Based Adsorption and Photocatalytic Approaches for Mitigation of Environmentally-Hazardous Pollutants—A Review. *J. Environ. Chem. Eng.* **2021**, *9*, 104879. [CrossRef]
64. Arabi, M.; Ostovan, A.; Li, J.; Wang, X.; Zhang, Z.; Choo, J.; Chen, L. Molecular Imprinting: Green Perspectives and Strategies. *Adv. Mat.* **2021**, *33*, 2100543. [CrossRef]
65. European Union. *Regulation (EU) 2019/1381 of the European Parliament and of the Council of 20 June 2019 on the Transparency and Sustainability of the EU Risk Assessment in the Food Chain and Amending Regulations (EC) No 178/2002, (EC) No 1829/2003, (EC) No 1831/2003, (EC) No 2065/2003, (EC) No 1935/2004, (EC) No 1331/2008, (EC) No 1107/2009, (EU) 2015/2283 and Directive 2001/18/EC*; European Union: Brussels, Belgium, 2019.
66. Karamfilova, E. *Food Contact Materials—Regulation (EC) 1935/2004*; European Parliamentary Research Service: Brussels, Belgium, 2016.
67. European Union. *EU Monitor Regulation (EU) 2015/2283 of the European Parliament and of the Council of 25 November 2015 on Novel Foods*; European Union: Brussels, Belgium, 2021.