Green Analytical Chemistry 16 (2026) 100330

Contents lists available at ScienceDirect

Green Analytical Chemistry

journal homepage: www.elsevier.com/locate/greeac

Green ultrasound-assisted extraction and GC-MS for the identification of intentionally and non-intentionally added substances in bio-based food contact materials

Maurizio Piergiovanni [a], Marco Fontanarosa [a], Nicolo' Riboni [a,b,*], Antonella Cavazza [a,b], Monica Mattarozzi [a], Federica Bianchi [a,b], Maria Careri [a]

[a] Department of Chemistry, Life Sciences and Environmental Sustainability, University of Parma, Parma 43124, Italy
[b] CIPACK (Interdepartmental Center for the Packaging), University of Parma, Parco Area delle Scienze 181/A, Parma 43124, Italy

ARTICLE INFO

Keywords:
Intentionally and non-intentionally added substances
Bioplastics
Food contact material
Analytical quality by design
Green solvents

ABSTRACT

The use of bioplastics as food contact materials (FCMs) is rapidly expanding as a sustainable alternative to conventional plastics, with polylactic acid (PLA) being among the most widely used biopolymer. The complex nature of bioplastics makes extraction and detection of intentionally and non-intentionally added substances (IAS and NIAS) particularly challenging, requiring the development of efficient and environmentally sustainable analytical procedures. In this study, a green analytical approach based on ultrasound-assisted extraction followed by GC–MS was developed for the untargeted analysis of GC-amenable IAS and NIAS from commercial biobased FCMs. For the first time in this context, Analytical Quality by Design principles were applied to optimize the extraction process. A screening design was applied to identify the significant critical method parameters, namely, solvent type, extraction and sonication time. A comparative assessment of conventional and green solvents was performed. Cyclopentyl methyl ether showed the highest extraction efficiency, while reducing the extraction time. The method operable design region ranged from 8:30 h to 10:50 h for extraction time and 10–25 min for sonication time. As a proof of concept, the optimized procedure was applied to bioplastic commercial items, leading to the detection of 39 volatile compounds belonging to different chemical classes. Multivariate data analysis allowed for a correct classification of samples according to their composition, demonstrating the method suitability for quality control purposes. Finally, AGREE, BAGI, and CHEMS-1 metrics were used to assess the greenness and applicability of the developed method, demonstrating a good alignment with the principles of green analytical chemistry

1. Introduction

Bioplastics have emerged as a viable alternative to conventional plastics, offering a sustainable and environmentally friendly alternative to fossil-based polymers. Polylactic acid (PLA), an aliphatic polyester deriving from renewable plant resources such as corn and starch, represents one of the most abundant biopolymers on the market: its European market share improvement is expected to upgrade from 31.0 % in 2023 to 43.6 % in 2028 [1]. PLA is currently used in many sectors, with primary application in food packaging for the production of films, cups, containers, and a wide range of rigid and flexible materials [2], as promoted by the EU Directive 2019/904 [3]. PLA offers several advantages, including biodegradability, biocompatibility, relatively low cost, and optical transparency. Despite these favorable attributes, it has some limitations compared to conventional petroleum-based polymers, particularly regarding the thermal resistance and mechanical performance at high temperatures. To address these issues, PLA is frequently blended with other biodegradable polymers, including polybutylene succinate (PBS), poly(butylene succinate-co-adipate) (PBSA), and polyhydroxyalkanoates (PHA), or combined with functional additives and/or active components to improve its properties [4].

However, the biobased origin of a material does not preclude the presence of potentially harmful compounds that could migrate into food and beverages [5]. In this context, the safety of bioplastics used as food contact materials (FCMs) is highly debated due to concerns about the presence of both intentionally added substances (IAS) and

* Corresponding author at: Department of Chemistry, Life Sciences and Environmental Sustainability, University of Parma, Parma 43124, Italy.
E-mail address: nicolo.riboni@unipr.it (N. Riboni).

https://doi.org/10.1016/j.greeac.2026.100330
Received 1 December 2025; Received in revised form 30 January 2026; Accepted 16 February 2026
Available online 16 February 2026
2772-5774/© 2026 The Author(s). Published by Elsevier B.V. This is an open access article under the CC BY-NC-ND license (http://creativecommons.org/licenses/by-nc-nd/4.0/).

non-intentionally added substances (NIAS), whose migration from bio-based items has been recently reported [6–8]. IAS, including monomers, starting substances, additives, polymer production aids, plasticizers, colorants and solvents, play a crucial role during manufacturing or in the final use of the product, as they enhance stability, improve mechanical properties, or extend the shelf life of food. NIAS. such as impurities, contaminants, and reaction or degradation products formed during the synthetic process, may also be present in FCMs, and their occurrence must be carefully evaluated. For a comprehensive risk assessment, the identification and quantitation of both IAS and NIAS in foodstuffs is necessary, involving material extraction or migration testing. To this aim, migration studies are usually performed according to European regulation [9]. However, as recently highlighted, there is still no harmonized legislation, nor have specific protocols been proposed for biopolymers [10].

To detect and identify unknown contaminants, mass spectrometry (MS)-based untargeted analytical approaches have been devised as essential tools to address emerging food safety concerns [7]. It is well-known that a comprehensive characterization of bioplastics requires the use of different analytical techniques, mainly based on gas chromatography (GC) and liquid chromatography (LC) approaches [10]. However, several studies have focused on the characterization of volatile/semi-volatile substances [8,11,12]. Since the concentration of compounds migrating into food simulants or leaching from plastic materials can be at trace levels, a wide range of extraction protocols has been proposed to enhance the release of both IAS and NIAS from bioplastics. In response to the need for more efficient extraction technologies, ultrasound-assisted extraction (UAE), microwave-assisted extraction (MAE) and accelerated solvent extraction (ASE), have emerged as valid alternative to solid-liquid extraction to enhance energy exchange and mass transfer process, thereby significantly reducing extraction time [13]. The extraction capability of various solvents has been evaluated, including methanol (MeOH) [8,14], ethanol (EtOH) [15], hexane (Hex), dichloromethane (DCM) [16], acetone (AcO) and toluene (Tol) [17], as well as solvent mixtures such as Hex/AcO [18] and DCM/EtOH [19].

Recently, green extraction methods have gained importance because of their sustainable and environmentally friendly nature. According to the principles of Green Analytical Chemistry (GAC) [20], great effort has recently been devoted to reduce or eliminate the use of toxic substances, minimizing waste and ensuring operator safety, thereby paving the way for the adoption of green solvents including ionic liquids [21], deep eutectic solvents [22], cyclopentyl methyl ether (CPME) [23], dioxolanes [24] and biobased EtOH. CPME is a sustainable alternative to traditional solvents such as Hex and DCM [16] due to its low environmental impact, increased safety, and efficient extraction performance. 1, 3-Dioxolane (Diox) exhibits CPME-like behavior [25] and has been proposed as green substitute for DCM and tetrahydrofuran. As for ionic liquids, they have been recently challenged, since various ionic liquids have been demonstrated to exhibit environmental toxicity [26]. Furthermore, shorter extraction times, lower organic solvent consumption, and higher yields of UAE, MAE, and ASE compared to conventional methods are advantageous for devising green sample preparation methods.

In this context, the application of Quality by Design (QbD) principles to analytical method development has attracted increasing attention. Analytical QbD (AQbD) provides a systematic framework for method development and is a valuable tool for optimizing extraction and separation procedures [27]. Based on Design of Experiments (DoE) and risk analysis, QbD principles enable a more efficient and reliable optimization process by elucidating the influence of multiple parameters (Critical Method Parameters, CMPs) on the analytical output (Critical Method Attributes, CMAs) and identifying the Method Operable Design Region (MODR), i.e. the multivariate space within which the analytical target is reliably achieved with a defined level of confidence [28]. AQbD has been applied to optimize the extraction of plasticizers from environmental samples [29], the chromatographic separation of isobaric polyphenols in food [30], and the development of an active food packaging material [31]. To our knowledge, this is the first time that AQbD is applied to the development of an extraction procedure in FCM analysis.

As part of the research activities related to the development of advanced extraction and analysis methods to determine hazardous chemical migration from food contact materials [32], the aim of this study was the development of a green, efficient, and reliable analytical procedure for GC profiling of extractables and leachables from bioplastic FCMs. To characterize the polymeric composition of commercial plastic samples, attenuated total reflection–Fourier transform infrared spectroscopy (ATR-FTIR) and differential scanning calorimetry (DSC) were also used. An extraction protocol based on UAE was optimized for the GC–MS determination of both IAS and NIAS according to the AQbD principles. The extraction capability of green solvents, namely CPME, Diox, and EtOH, was compared with that of conventional solvents, including isooctane (Iso), Tol, and ethyl acetate (EtAc). Multivariate data analysis, i.e. Principal Component Analysis (PCA) and Linear discriminant Analysis (LDA), was applied to highlight the GC-amenable compounds characterizing the different bioplastic materials. The greenness of the proposed approach was assessed using the Analytical GREEnness calculator (AGREE) [33] together with the evaluation of the hazard values associated with the green and traditional solvents used in this study [34]. Finally, the applicability of the developed method was also evaluated using the Blue Applicability Grade Index (BAGI), in accordance with the practical aspects of white analytical chemistry [35].

2. Experimental section

2.1. Chemicals and materials

Tol (99.8 % purity), EtOH (96 % purity), CPME (99.9 % purity), Diox (99.9 % purity) were purchased from Carlo Erba Reagents (Milan, Italy). Isooct (99.5 % purity) was from Labscan analytical sciences (Gliwice, Poland), while EtAc (99.7 % purity) from Sigma-Aldrich (Milan, Italy). Pentadecane (C_{15}), hexadecane (C_{16}), heptadecane (C_{17}), octadecane (C_{18}), nonadecane (C_{19}), eicosane (C_{20}), heneicosane (C_{21}), docosane (C_{22}), tricosane (C_{23}), tetracosane (C_{24}), pentacosane (C_{25}), hexacosane (C_{26}), heptacosane (C_{27}), octacosane (C_{28}), nonacosane (C_{29}) and triacontane (C_{30}) all >99 % purity were purchased from Merck (Milan, Italy). Dibutyl phtahalate (99 % purity), diisobutyl phtahalate (99 % purity), hexadecanoic acid (>99 % purity), octadecanoic acid (95 % purity), erucamide and polytetrafluoroethylene (PTFE) syringe filters (0.2 μm) were from Merck.

To avoid environmental contamination, glass or stainless-steel apparatus was used. Prior to use, all glass apparatus was soaked in 10 % HCl for 12 h, rinsed with milliQ water, maintained at high temperature for 6 h, and rinsed with MeOH.

2.2. Samples

A total of 25 bioplastic household items including 18 cutlery samples, 2 bowls, 2 packages of straws, 6 cups, and 1 pack of coffee stirrers from various manufacturing companies were purchased from local markets (Table S1). Prior to analysis, all samples were ground using an A11 basic analytical mill (IKA, Staufen, Germany) in the presence of liquid nitrogen. The resulting powders were collected in glass tubes and stored at –80 °C until extraction. Pooled samples prepared by mixing 500 μL of individual extracts were used as quality controls (QCs) and analyzed in duplicate every 5 chromatographic runs.

2.3. Material characterization

ATR-FTIR spectra of the analyzed samples were collected in a 4000–400 cm^{-1} range using a Spectrum Two FTIR spectrophotometer (PerkinElmer, Shelton, CT, USA). An average of 16 scans and a

resolution of 2 cm^{-1} were set. Each sample was analyzed in triplicate.

DSC analysis was performed using a DSC 6000 (Perkin Elmer, Waltham, MA, US). Five mg of each sample were heated from 30 °C to 200 °C at 10 °C/min under nitrogen. The degree of crystallinity was calculated using the following equation:

$$X_c = \left(\Delta H_f - \Delta H_c\right)/93$$

where ΔH_c and ΔH_f represent the crystallized and fused enthalpy of samples, respectively, and 93 J/g is attributed to the tabulated fused enthalpy of 100 % crystalline PLA [36].

2.4. Optimization of ultrasonic assisted extraction

The chromatographic responses of hexadecanoic acid, octadecanoic acid, hexadecanoic acid 2-hydroxy-1-(hydroxymethyl)ethyl ester, octadecanoic acid 2-hydroxy-1-(hydroxymethyl)ethyl ester, and di(2-ethylhexyl) sebacate (DOS) were selected as CMAs [29]. A screening design was applied by evaluating the effect of two quantitative factors, namely extraction time (Ext. time, i.e. the time during which the sample was put in contact with the solvent without ultrasound treatment) and ultrasonic time (UAE time, i.e. the time during which ultrasounds were applied), and one qualitative factor, i.e. solvent type (Solv. type), used as CMP [29]. Ext. time in the 4–14 h range and UAE time in the 15–45 min range were considered as design space (Table S2). The use of conventional and green solvents was investigated: two different experimental matrices were considered, one for conventional solvents (Tol, EtAc, and Isoct) and the other for green solvents, namely CPME, Diox, EtOH. A symmetric screening matrix was applied. The ratio between the amount of sample and the volume of extraction solvent was set to 20, in agreement with previously published studies [17,37]. After evaluating the significant factors, the Response Surface Methodology (RSM) was applied using a Face Centered Composite Design (CCF) to select the optimal extraction conditions and identify the MODR through Monte-Carlo simulations [38]. The following experimental domain was considered for CCF: Ext. time 7–11 h, UAE time 5–25 min. The experimental error was evaluated by performing five replicates at the center of the experimental domain. To obtain a good compromise for all the CMAs, the minimum values were calculated as 70 % of the maximum responses, which were considered as target. A defect per million opportunities (DPMO) target of 100,000 was set for the risk analysis, equivalent to a 10 % error probability [29]. Data were processed using MODDE 13 software (Sartorius Data Analytics AB, Göttingen, Germany).

The optimized extraction procedure was then applied to all investigated samples: 0.2 g of sample was weighed in a test tube and 4 mL of CPME were added [17]. The tube was closed, covered with aluminum foil, and submitted to the UAE using an ultrasonic bath (J.P. Selecta, Barcelona, Spain) at room temperature and 100 % power. Once the extraction was completed, the extract was centrifuged, filtered on 0.2 μm PTFE syringe filters, and submitted to GC–MS analysis.

QC samples prepared by mixing equal volumes of each extract were used to evaluate retention time (RT) precision and method precision based on the responses associated with the CMAs. Both RT precision and method precision were evaluated in terms of repeatability (assessed through 5 independent replicate measurements performed within the same day) and intermediate precision (assessed through the same number of independent replicates, conducted over three consecutive days) by calculating relative standard deviations (RSD %). Intermediate precision was estimated verifying homoscedasticity of data and performing the analysis of variance (ANOVA) at a 95 % confidence level. Finally, the selectivity of compound annotation was verified by comparing the annotations from a single-item extract with those from the QC samples.

2.5. GC-MS analysis

Details on the GC-MS operating conditions are reported in the Supplementary Material.

2.6. Data analysis

The annotation of volatile compounds was carried out by matching the experimental mass spectra with the best fitting spectra available in both the Wiley 275 and the NIST17 (National Institute of Standards and Technology) databases.

Retention indices (RIs) were determined using a series of n-alkanes ranging from C_{15} to C_{30} as reference compounds, according to the following equation:

$$RI = 100z + 100(RT_i - RT_z)/(RT_{z+1} - RT_z)$$

where:

- RI is the retention index of the unknown compound
- RT_i is the retention time of the unknown compound
- RT_z and RT_{z+1} are the retention times of the n-alkanes eluting directly before and after the unknown compound, respectively
- z corresponds to the number of carbon atoms in the n-alkane eluting just before the unknown compound

The calculated RIs were compared with those stored in a proprietary database [39] or available in the literature [40]. Pure standards of 1-dodecanol, hexadecane, heptadecane, octadecane, nonadecane, hexadecanoic acid, dibuthyl phthalate, bis-methoxyethyl phthalate, heneicosane, methyl octadecanoate, octadecanoic acid, and erucamide were injected for confirmatory purposes.

As a proof of concept, PCA and LDA were performed on chromatographic peak areas. Data were autoscaled to mean zero and unit variance. Data filtering was performed by removing variables present in less than 30 % of the investigated samples. PCA was carried out to explore data trends within samples, whereas LDA was performed to distinguish the volatiles responsible for the discrimination of the investigated bioplastic items. A k-fold ($k = 5$) cross-validation was applied to obtain the figure of merits of the developed model.

2.7. Greenness assessment

The compliance with the GAC principle was estimated using the AGREE metric approach [33] and by calculating the hazard values of the green and traditional solvents used in the study. The values reported on the corresponding safety data sheets were used as reference values [34,41]. Finally, the BAGI approach was applied to integrate analytical and practical performance criteria to environmental ones [35].

3. Results and discussion

3.1. Material characterization

ATR-FTIR spectroscopy (Fig. S1) and DSC (Fig. S2) were preliminary used for the characterization of the biobased items. ATR-FTIR spectra confirmed that the investigated samples were based on different bioplastic materials, with most of the spectra consistent with PLA. The carbonyl ester (C=O) stretching band was used as the most discriminating feature for a rapid identification of the main component. Eighteen samples out of 25 were identified as PLA (Table S1), according to the following typical bands [42,43]: 1748 cm^{-1} stretching C=O for the crystalline phase vs 1758 cm^{-1} for the amorphous phase; 3000–2940 cm^{-1} (2997 and 2939 cm^{-1} stretching asymmetric and symmetric CH_3), 1453 cm^{-1} (asymmetric bending CH_3), 1383 cm^{-1} (symmetric bending CH_3), 1265–1047 cm^{-1} (stretching C–O–C), 870 cm^{-1} (absorption of

O–CH–CH_3) and 757 cm^{-1} (wagging α-CH_3).

DSC analysis was also performed to support the results obtained by ATR-FTIR and to assess the compliance of the PLA items with the specifications (crystallized or not crystallized item) indicated on their labels. The results showed a good agreement with the declared information (Table S1).

3.2. Screening design

A preliminary screening design was applied to optimize the extraction conditions for the determination of extractable and leachable compounds from FCMs. The choice of CMAs was based on their distinct retention times, ranging from 10.96 to 21.73 min, and spaced approximately 3–5 min apart, thus covering most of the chromatographic window and representing the physical and chemical diversity in terms of FCM extractables. Considering the broad range of potential contaminants that can be migrate from household items, and the varying extraction efficiencies of various solvents, the initial phase of the study aimed to identify the most significant extraction parameters, namely, solvent type, extraction time, and sonication time. A sample weight/extraction volume ratio of 20 was chosen in accordance with recent literature, which reports that increasing the extraction solvent volume does not lead to significant differences in analytical performance. In addition, preliminary evaluations proved the absence of significant changes in the chromatographic responses when minor adjustments in solvent volume were tested. Finally, it is notheworthy to mention that the proposed protocol aligns well with the principles of GAC, since this study used a downscaled version of the established procedure. A

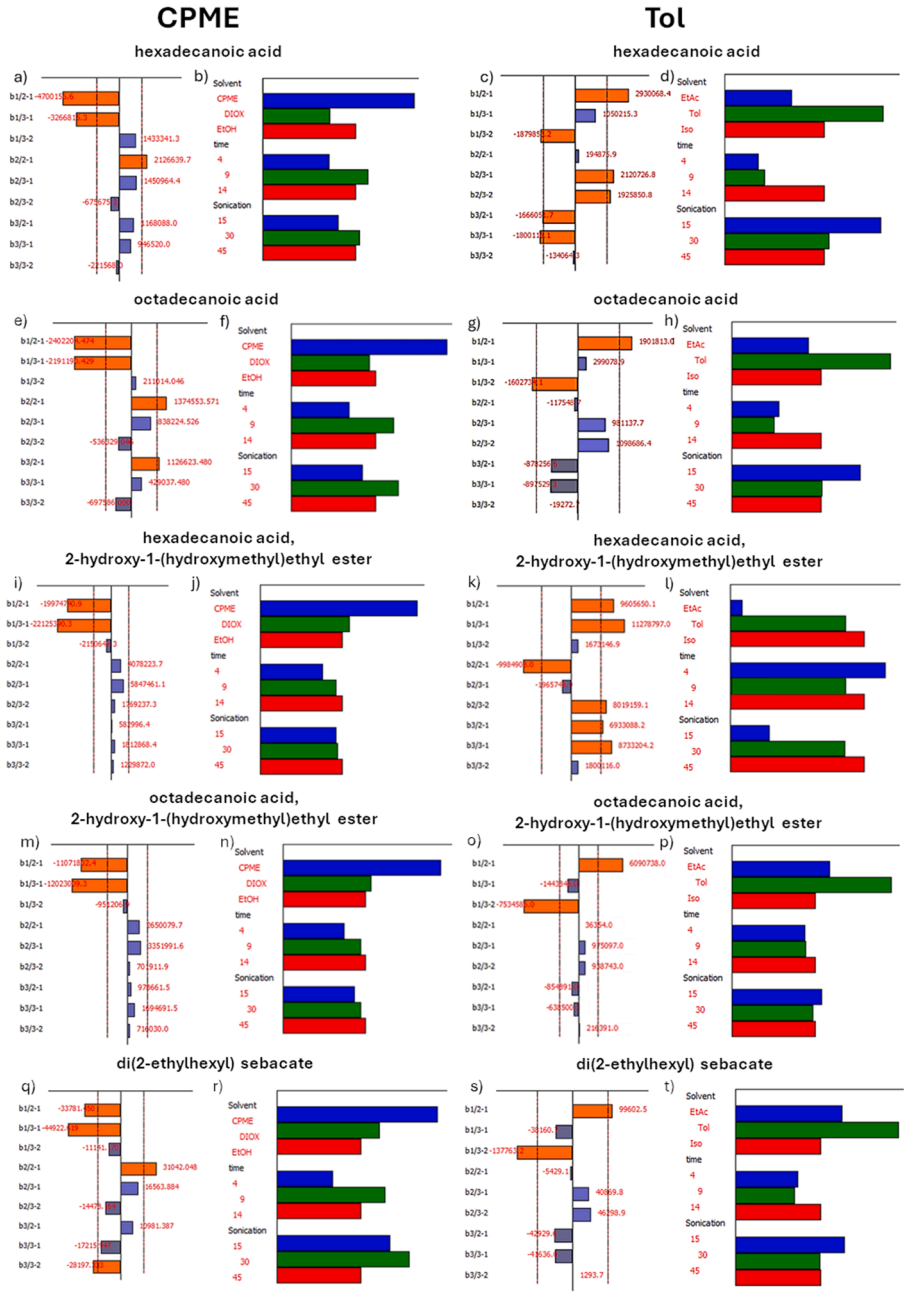


Fig. 1. Screening design for CPME and Tol: effects of hexadecanoic acid (a,b,c,d); octadecanoic acid (e,f,g,h); hexadecanoic acid, 2-hydroxy-1-(hydroxymethyl)ethyl ester (i,j,k,l); octadecanoic acid, 2-hydroxy-1-(hydroxymethyl)ethyl ester (m,n,o,p), and di(2-ethylhexyl) sebacate (q,r,s,t). Statistically significant effects are colored in orange. In (b,d,f,h,j,l,n,p,r,t) the bar length is related to the effect of single levels on the response.

comparative assessment of conventional and green solvents was performed to evaluate their extraction capability. Fig. 1 (a,c,e,g,i,k,m,o,q,s) shows the graphical analysis of the model coefficients, where each bar represents the magnitude of a specific effect corresponding to a change between two defined levels. For example, b1/2–1 shows the magnitude of the effect size of first critical method parameter (i.e. solvent type) when its level is changed from low (1) to medium (2).

The results obtained from this screening design not only allowed us to identify the significant factors to consider in the factorial design but also provided a more focused insight into the experimental domain to be explored in the subsequent step. The graphical analysis of the results (Fig. 1) enabled the identification of the conditions that maximize the extraction capability of the CMAs. Among the green solvents, CPME was the most effective for the extraction of all model compounds. Regarding the Ext. time, the intermediate level (corresponding to 9 h) was optimal for hexadecanoic acid, octadecanoic acid, and DOS, while no significant differences were observed for the other compounds. Finally, a UAE time of 30 min significantly improved the extraction of octadecanoic acid alone. Based on these findings, the following conditions were selected for green solvents: CPME as the extraction solvent, an Ext. time of 9 h, and an UAE time of 15 min.

Among conventional solvents, Tol provided the highest responses for all analytes except for hexadecanoic acid 2-hydroxy-1-(hydroxymethyl) ethyl ester. For this compound, no significant difference was observed between Tol and Iso. Ext. time was not a significant factor for most compounds, with the exception of hexadecanoic acid and its methyl ester, for which 14 h generally provided the best results. As for UAE time, no significant effect was observed for any of the CMAs except for hexadecanoic acid 2-hydroxy-1-(hydroxymethyl)ethyl ester, for which a 30 min sonication resulted in improved extraction efficiency. Considering that 15 min were sufficient to effectively extract most of the analytes, this UAE time was chosen as the best compromise for the simultaneous extraction of extractable and leachable compounds. In summary, the optimal conditions for conventional solvents were Tol as the solvent, an Ext. time of 14 h and a UAE time of 15 min. Under these conditions, no significant difference was observed in either the number peaks or the GC responses of the extracted compounds when CPME was used as the extraction solvent compared to Tol (Fig. S3), indicating comparable extraction performance.

Taking into account the need to develop a more environmentally friendly approach with potentially shorter extraction times, CPME was selected as the most suitable solvent. Accordingly, the experimental domain for further optimization using a CCF design was set as follows: Ext. time: 7–11 h, UAE time: 5–25 min. Chromatographic separation was carried out using a 5 % phenyl/95 % methyl-polysiloxane GC column, selected for its broad applicability.

Excellent retention time precision was observed in terms of both RT repeatability and RT intermediate precision, with RSD always lower than 0.5 %. Very good results were also achieved in terms of method precision with RSD always lower than 8 %. ANOVA did not show significant differences ($p > 0.05$) among the mean responses obtained over 3 days. Considering that independent replicate measurements were performed and that the volatile mixtures present in biopolymers are highly complex, the achieved results demonstrate the reliability of the developed procedure. Finally, no problems in compound identification were observed comparing the annotation from a single-item extract with those from the QCs, thus proving method selectivity.

3.3. Optimization of ultrasonic assisted extraction of IAS and NIAS with response surface methodology

Applying the CCF, all the calculated models were statistically significant ($p < 0.05$). The coefficients of determination R^2 ranged from 0.84 to 0.92, while the predicted variation coefficients Q^2 were in the 0.65–0.72 range. No lack-of-fit was observed for any of the models. These findings highlighted the goodness of fit and the good predictive capability in cross-validation for all the considered models. The coefficient plot is reported in Fig. S4 and the response surfaces for each CMP are depicted in Fig. S5.

Ext. time had a positive effect on the responses of all investigated compounds, while UAE time showed a significant positive effect on octanoic acid, hexadecanoic acid 2-hydroxy-1-(hydroxymethyl)ethyl ester and octadecanoic acid 2-hydroxy-1-(hydroxymethyl)ethyl ester. No significant interaction was observed. As for Ext. time, negative quadratic effects were calculated for all the compounds; finally, octanoic acid, hexadecanoic acid 2-hydroxy-1-(hydroxymethyl)ethyl ester, and octadecanoic acid 2-hydroxy-1-(hydroxymethyl)ethyl ester were characterized by a negative quadratic effect with respect to the UAE time. The contour plots for each CMA are shown in Fig. 2, where the regions corresponding to the response maximization are colored in red. Overall, the best results were achieved when both Ext. time and UAE time were set at intermediate levels. These findings were further confirmed by the sweet spot plot depicted in Fig. S6, which illustrates the areas where all response criteria are simultaneously met based on the overlay of the individual contour plots.

The MODR, i.e. the region where the methods provide reliable results, was defined by considering both the predicted mean values of the CMAs and the probability of meeting the CMA, integrating data from the predictive models with Monte Carlo simulation results. The risk of failure was plotted on the probability map shown in Fig. 3. The MODR was determined starting from a robust point corresponding to 9 h:45 min for Ext. time and 19 min for UAE time. The optimal setpoint was 9 h:43 min and 18 min as Ext. time and UAE time, respectively. The MODR range was as follows: Ext. time: 8 h:30 min–10 h:50 min; UAE time: 10–25 min. The region was validated using a Plackett-Burmann design and the results confirmed that the CMA targets were met. These findings demonstrate that satisfactory outcomes can be achieved even when operating at the lower boundaries of the MODR, thus allowing for a reduction in overall analysis time. A comparison of the operating conditions used in this study with those reported in the literature is summarized in Table 1. In all studies, except for Pitirollo et al. [15], only traditional solvents were used, and in larger quantities. Overall, UAE is a simple and cost-effective extraction technique that reduces solvent consumption and sample preparation time. In our study, the use of short UAE time intervals allowed for a close control of the extraction temperature, which is a critical aspect since prolonged sonication can cause a temperature increase that may affect the extraction performance and compound stability. The proposed UAE GC–MS method also offers additional advantages over GC–HRMS-based approaches. GC–MS provides sufficient sensitivity and selectivity for routine analysis, while benefiting from lower operating and maintenance costs, greater availability, and easier method use compared to GC–HRMS. Although GC–HRMS offers higher resolving power and superior mass accuracy, it requires greater expertise and resources, including energy consumption, which results in lower scores in both BAGI and AGREE metrics. In contrast, GC–MS does not require highly trained personnel, and benefits from extensive commercial spectral databases, reducing the need for home-made libraries. Overall, the proposed approach represents a robust and practical alternative for high-throughput and routine analytical applications without the need for highly specialized instrumentation.

3.4. Identification of volatile compounds and multivariate data analysis

The extraction of extractable and leachable compounds from FCMs was carried out under the optimized conditions. A typical UAE-GC–MS chromatogram is reported in Fig. S7. In total, 39 GC-amenable substances belonging to different chemical classes were detected in at least two samples of each household category (Table S3). Compounds were considered positively identified when both the mass spectra and retention indices matched, allowing for a tolerance of 15 RI units compared to values reported in online databases, considering possible variations due

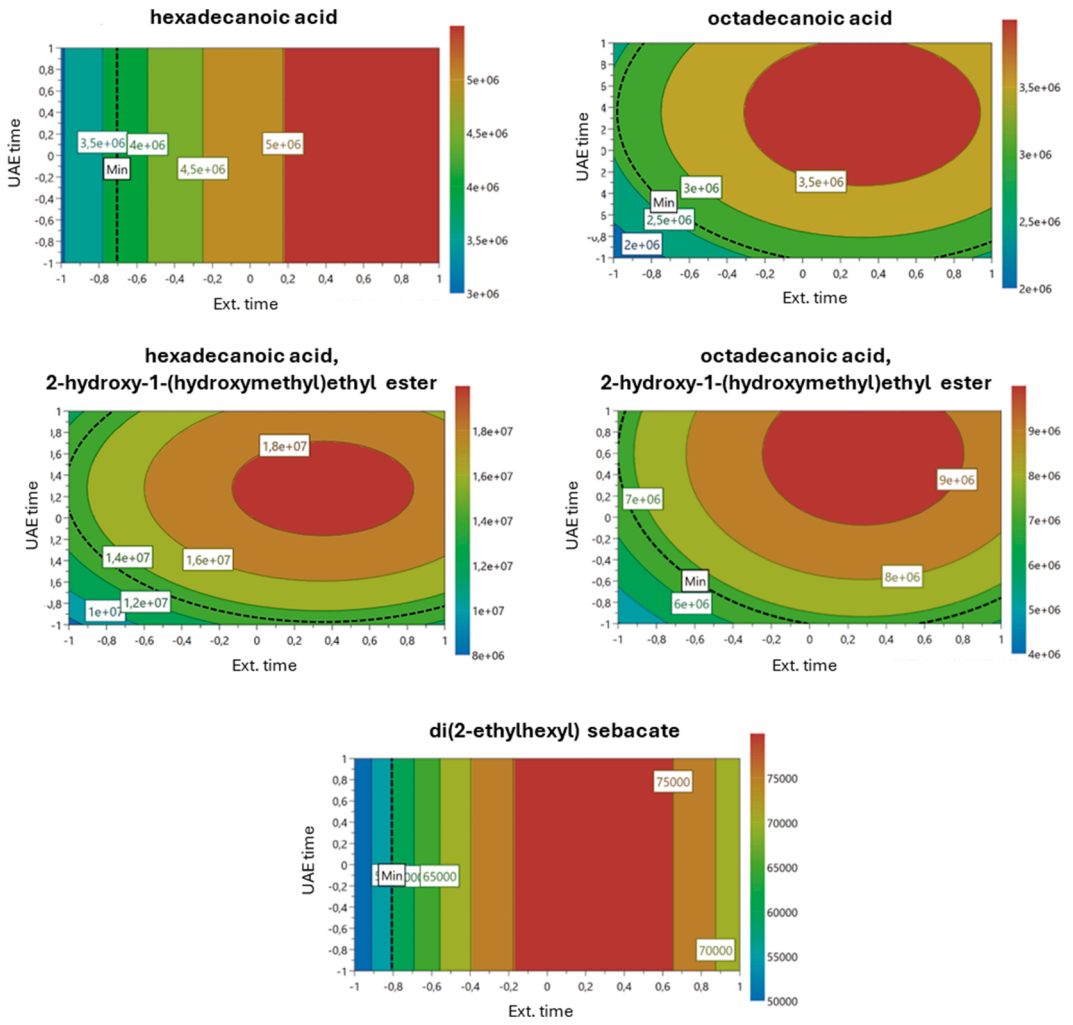


Fig. 2. RSM contour plots of the CMAs as a function of extraction time and UAE time.

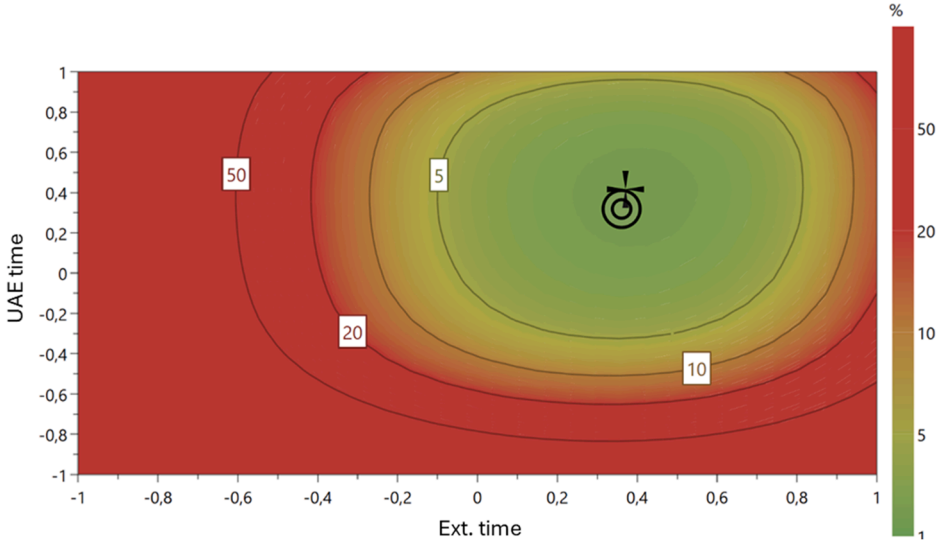


Fig. 3. Probability map as a function of UAE time and Ext. time. The MODR is included in the 10 % isoprobability line; the cross indicates the robust point, the circles is the optimal setpoint.

to different columns and operating conditions. Pure standards were injected for confirmatory purposes, providing increased confidence in compound identification. Examples of spectral comparison are shown in Fig. S8. It should be noted that, because reference standards are limited,

Table 1
Comparison of the operating conditions used in the present study with those reported in previous studies for the determination of IAS and NIAS in PLA-based samples.

Solvent	Sample amount (g)	Volume (mL)	Extraction time (h)	Extraction technique	Analytical platform	Ref
MeOH	3	20	1	UAE+preconcentration	UPLC—HRMS	[8]
Acetonitrile	0.8	5	24	solid/liquid	GC—HRMS	[12]
MeOH	0.2	10	24	solid/liquid	TD-GC–MS/MS	[14]
EtOH	3	20	1	UAE+preconcentration	GC-MS, HPLC-MS	[15]
MeOH, AcO, Tol	0.5	30	1	UAE+preconcentration	UHPLC-(HESI)HRMS	[17]
Hex/AcO	2	10	Overnight	solid/liquid+ preconcentration	UHPLC-(HESI)HRMS	[18]
DCM, EtOH	0.25	12	01:15	Dissolution UAE+precipitation	UPLC-MS	[19]
DCM, EtOH	0.25	12	02:30	Dissolution+UAE/ reprecipitation	GC–MS, GC—O-MS, APGC-QTOF	[44]
MeOH	1	5	24	solid/liquid+ preconcentration	GC–MS	[45]
CPME	0.2	4	09:40	solid/liquid+UAE	GC-MS	This study

many IAS and most NIAS are absent from spectral libraries: as a result, some compounds remain unidentified or can only be assigned to a general chemical class. Among the identified compounds, phthalates represent a well-know and ubiquitous class of plasticizers [46]. In our study low-intensity signals corresponding to diisobutyl, dibutyl phthalate and bis-methoxyethyl phthalate were detected. DOS, another plasticizer belonging to the chemical class of sebacates commonly used in the production of plastic material was identified.1,6-Dioxacyclododecane-7,12-dione, the cyclic oligomer of butylene adipate, was also observed. This compound has previously been detected by Coralli et al. [47] as a pyrolysis product of PBAT, and as NIAS in both plastic compostable plastic bags and adhesives used in laminated bioplastics [48]. Tributyl (Z)-prop-1-ene-1,2,3-tricarboxylate is a recognized impurity resulting from the hydrolysis of acetyl tributyl citrate, a green and safer alternative to phthalate plasticizers, which is frequently used in the production of biobased items [49]. Owing to their good compatibility with polar polymers, citric acid esters are widely evaluated as environmentally friendly plasticizers in PLA-based bioplastics [50].

Phosphorous acid, triphenyl ester (i.e. triphenyl phosphite) is not an authorized additive in EU Regulation 10/2011 for food contact materials [9], whereas EFSA has established that phosphorous acid, triphenyl ester polymer with α-hydro-ω-hydroxypoly[oxy(methyl-1,2-ethanediyl)], $C_{10–16}$ alkyl esters can be used as an additive in FCMs, for the production of food contact polyolefins [51]. In addition, triphenyl phosphite has been reported to be intentionally used as chain extender in the production of polyesters and polyester-based composites to increase polymer molecular weight [52]. These findings suggest that its presence in biobased items could be attributed to several factors, including the use of polyolefins in the formulation of the biobased products, cross-contamination during the recycling or waste stream or potentially as a result of its unauthorized addition in the formulations of bioplastics intended for food contact applications. As for phosphoric acid, triphenyl ester (triphenyl phosphate), it is a frequently used flame retardant in many polymers including PLA/polycarbonate composites [53], but it can be also used as plasticizer exerting a positive effect on PLA crystallization [50].

7,9-Di-tert-butyl-1-oxaspiro(4.5)deca-6,9-diene-2,8-dione is a recognized degradation product of Irganox-type antioxidants [54], while hexadecanoic acid, octadecanoic acid, their corresponding methyl esters and erucamide are typically added as lubricants or slip agents in plastic formulations [12,55].

A variety of alkanes were also identified. Their presence can be explained considering that these compounds are natural constituents of plants [56], although they can also originate from polyolefins. These findings suggest that their occurrence could arise from cross-contamination during recycling process, particularly when mixed plastic waste streams are involved [55]. Another possible explanation is the intentional addition of small amounts of polypropylene or polyethylene during PLA manufacturing to enhance its mechanical properties.

As a proof of concept, exploratory PCA was initially carried out to evaluate sample clustering and identify relationships among samples. The first four PCs accounted for 66.8 % of variance, but no significant grouping among samples was observed, except for the presence of sample P10, totally isolated at positive PC1 values (Fig. S9a) due to the high amount of aliphatic and aromatic hydrocarbons, and methyl palmitate (Fig. S9b). Better results were obtained after its removal from the dataset, since a partial clustering of the samples was observed in the PC_1 *vs* PC_2 (of the total variance) and in the PC_1 *vs* PC_4 space, explaining 37.1 % and 34.2 % of the total variance respectively (Fig. S10). Similarly, LDA was applied in order to evaluate which volatile compounds could be responsible for the classification of the samples according to their main plastic component (PLA, cPLA and noPLA). As shown in Fig. 4a, three distinctive groups were observed, with good results in terms of sensitivity, specificity and precision (Table S4) [57]. The most significant variables for discriminating the groups were those characterized by the highest standardized discriminant coefficients (Fig. 4b). Among these, acetyl tributyl citrate, erucamide, methyl stearate, 7,9-di-tert-butyl-1-oxaspiro(4.5)deca-6,9-diene-2,8-dione, triphenyl ester phosphouros acid and triphenyl phosphate showed negative values in CV1, thus characterizing the profile of cPLA. Discrimination between amorphous PLA and no-PLA based products was observed according to CV2, with hexadecenoic acid and hexadecanoic acid 2-hydroxy-1-(hydroxymethyl)ethyl ester present at higher amounts in no-PLA samples. By contrast, the citric acid ester (RT 13.6 min), bis-methoxyethyl phthalate and heptadecane were positively related with PLA-based objects. As previously stated, these findings should be considered as preliminary investigation due to the small sample size. Future studies applying the developed method to a larger cohort of bioplastic items should allow for more robust and generalizable conclusions.

3.5. *Evaluation of the UAE-GC–MS method by greenness metrics*

Alignment with the GAC framework is fundamental for the development of new analytical green protocols that are both efficient and environmentally sustainable.

The greenness of the developed UAE-GC–MS method was first evaluated using the AGREE tool [33] by comparing the results obtained with CPME with those obtained with Tol. Total scores of 0.59 and 0.48 were obtained for CPME (Fig. 5a) and Tol (Fig. 5b), respectively. Considering that the performance of the procedure is illustrated by the color assigned to each segment, and that each segment is labeled with the number of the corresponding assessment criterion, positive outcomes were observed for both solvents in terms of the low amount of sample required (0.2 g), the reduced number of sample preparation steps (3), the degree of process automation, the absence of derivatization, and the determination of multiple analytes within a single run (39). The main critical aspects were related to the device positioning, which is off-line, and to the relatively high energy consumption associated with the use of GC–MS. A further drawback was associated to the use of CPME which is considered a green but not-biobased solvent. For this reason, principle n.10 of the AGREE tool was negative (red color) for both CPME and Tol.

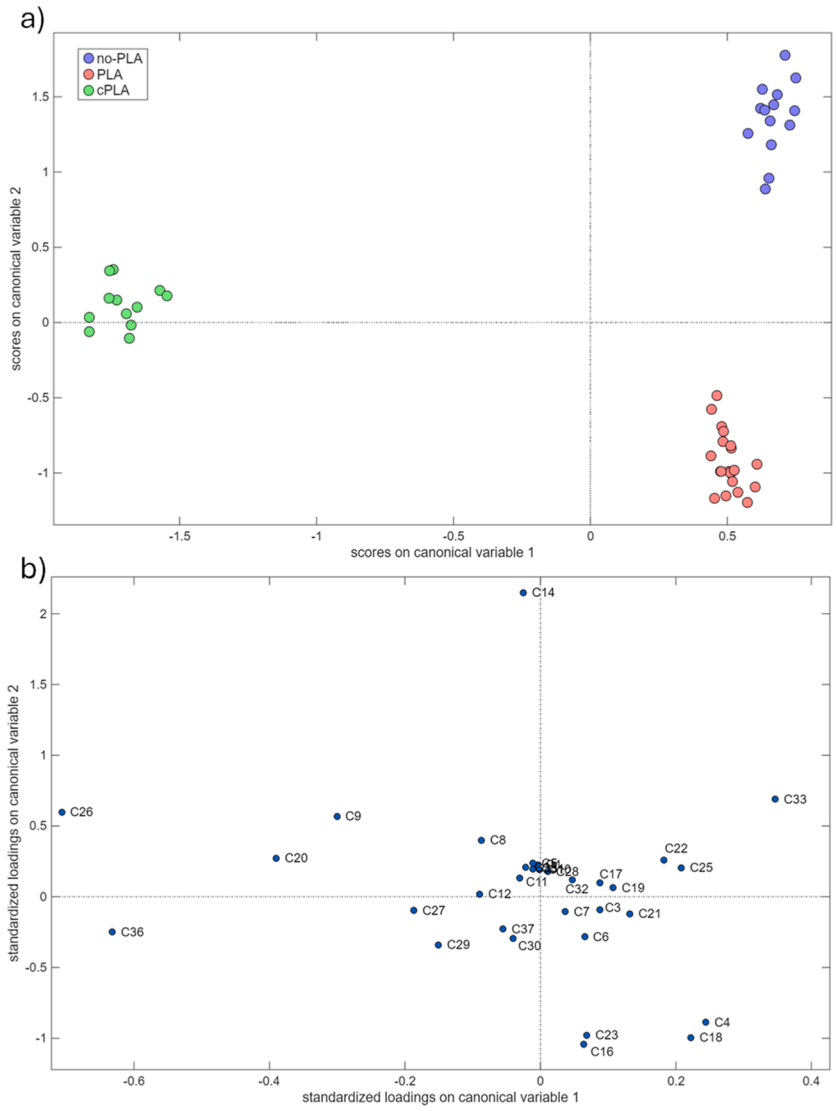


Fig. 4. LDA analysis: a) score plot and b) standardized loading plot of canonical variables 1 and 2.

However, replacing Tol with CPME had a positive impact on both solvent toxicity and operator safety.

In addition to the AGREE metric, the CHEMS-1 model was applied to provide a complementary assessment of the environmental and health impacts associated with replacing Tol with CPME. CHEMS-1 evaluates the effect of solvents based on multiple criteria, including toxicity to both animals and humans, bioaccumulation potential, biodegradability, and environmental persistence, offering a quantitative perspective on both ecological and operator safety considerations [34]. Using this approach, tHV values of 24.1 and 48.3 were obtained for CPME and Tol, respectively. In particular, Tol is associated with a higher hazard value for chronic noncancer toxicity due to its neurotoxic effects, and its adverse impacts on the kidneys, liver, and respiratory system. Additionally, Tol exhibits a greater environmental impact, primarily due to its higher acute and chronic toxicity to aquatic organisms: taHV values of 31.8 and 65.8 were obtained for CPME and Tol, respectively, indicating that CPME has a markedly lower overall hazard profile compared to Tol.

Finally, the BAGI tool was applied to assess the practical applicability of the developed analytical procedure [35]. As shown in Fig. 5c, a score of 70 was obtained, indicating that the proposed UAE-GC–MS method complies with the principles of GAC while maintaining a good operational feasibility. The lowest score (2.5) was associated with the type of analysis (qualitative) as indicated by the white segment of the pictogram, whereas high scores (score 10) were obtained for the following attributes (dark blue color in the pictogram): multi-element analysis for >15 compounds; commonly available reagents; no-preconcentration required and amount of sample. This result highlights that the procedure is not only environmentally sustainable but also readily implementable in routine laboratory settings without the need for advanced equipment or complex instrumentation. The combination of a favorable BAGI score and the positive AGREE evaluation confirms the applicability and sustainability of the developed approach, reinforcing its potential for widespread adoption in the analytical practice.

4. Conclusion

A green, efficient and reliable UAE-GC–MS method was developed to profile extractables and leachables from bioplastics used as FCMs. For the first time in this field, a QbD approach was applied to optimize the extraction conditions. By integrating screening design, response surface methodology, and Monte Carlo simulation in a comprehensive experimental approach, a robust and efficient protocol was established using CPME as a greener alternative to conventional solvents. CPME was able to effectively extract IAS and NIAS from bioplastics in shorter contact times compared to toluene, thus reducing analysis time while

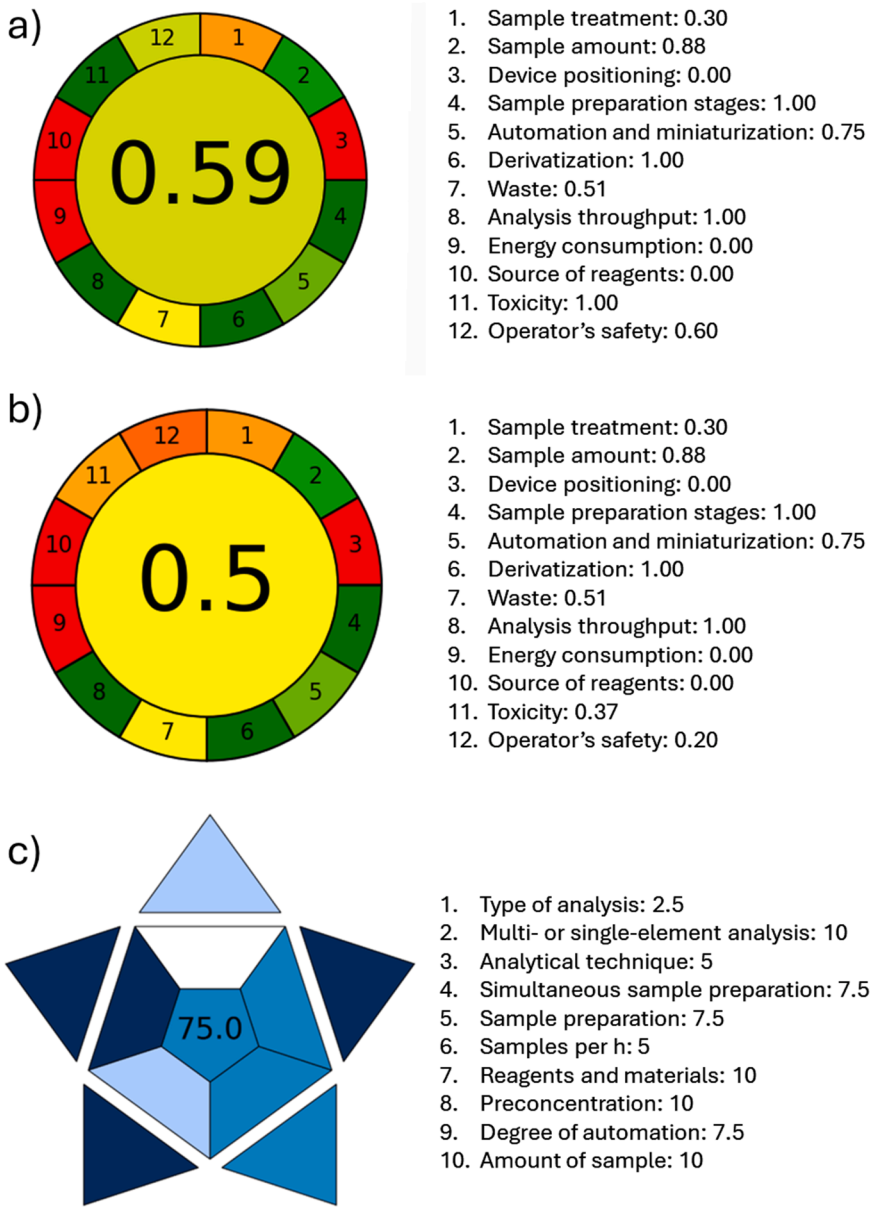


Fig. 5. Analytical method greenness profiles of the developed UAE-GC–MS procedure according to the AGREE metric for a) CPME, b) Tol; c) pictogram obtained using BAGI. The scores for each principle are reported alongside.

maintaining high extraction efficiency. The identification of the MODR ensured both analytical reliability and optimal extraction performance. As a proof of concept, the developed method was applied to the analysis of commercial items made of PLA, cPLA, and other bioplastic materials. The identified volatiles include different classes of compounds that can act as plasticizers, lubricants, or other additives. Degradation products of antioxidants were also identified. Multivariate data analysis allowed for a correct classification of the samples according to their composition demonstrating the suitability of the method for quality control purposes. A strong alignment with the principles of GAC was also demonstrated, achieving positive results both in terms of analytical performance and environmental sustainability. The combined use of AGREE, BAGI, and CHEMS-1 tools provided a comprehensive evaluation of the method's greenness, applicability, and safety, confirming the benefits of replacing conventional solvents with greener alternatives. Overall, the study highlights the potential of the proposed methodology as a reliable and environmentally friendly alternative suitable for routine laboratory implementation.

CRediT authorship contribution statement

Maurizio Piergiovanni: Writing – review & editing, Visualization, Formal analysis, Data curation, Conceptualization. **Marco Fontanarosa:** Writing – original draft, Formal analysis. **Nicolo' Riboni:** Writing – review & editing, Writing – original draft, Visualization, Methodology, Formal analysis, Data curation. **Antonella Cavazza:** Writing – review & editing, Writing – original draft, Methodology, Data curation, Conceptualization. **Monica Mattarozzi:** Writing – review & editing, Methodology, Data curation. **Federica Bianchi:** Writing – review & editing, Writing – original draft, Visualization, Supervision, Methodology, Data curation, Conceptualization. **Maria Careri:** Writing – review & editing, Supervision, Funding acquisition, Conceptualization.

Declaration of competing interest

There are no conflicts to declare.

Acknowledgements

This research is in the framework of "Research and innovation network on food and nutrition Sustainability, Safety and Security–Working ON Foods" (ONFOODS) project which received funding from the National Recovery and Resilience Plan (NRRP) and the Mission 4 Component 2 Investment 1.3-Call for tender No 341 of 15/03/2022 of the Italian Ministry of University and Research funded by the European Union–NextGenerationEU. Award Number: Project code PE0000003, Concession Decree No 1550 of 11/ 10/2022, adopted by the Italian Ministry of University and Research, CUP D93C22000890001 for technical support.

The authors acknowledge the COMP-R Initiatives, funded by the "Departments of Excellence" program of the Italian Ministry for University and Research (MUR, 2023–2027).

Supplementary materials

Supplementary material associated with this article can be found, in the online version, at doi:10.1016/j.greeac.2026.100330.

Data availability

Data will be made available on request.

References

[1] European Bioplastics, European Bioplastics, 2024. https://www.european-bioplastics.org/market/ (accessed October 13, 2025).
[2] L. Mou, J. Li, Y. Lu, G. Li, J. Li, Polylactic acid: a future universal biobased polymer with multifunctional performance—from monomer synthesis, and processing to applications: a review, J. Hazard. Mater. Adv. 18 (2025) 100757, https://doi.org/10.1016/j.hazadv.2025.100757.
[3] European Council, Directive (Eu) 2019/904 of the European Parliament and of the Council of 5 June 2019 on the Reduction of the Impact of Certain Plastic Products on the Environment, 2019. https://eur-lex.europa.eu/eli/dir/2019/904/oj/eng.
[4] S. De Luca, D. Milanese, D. Gallichi-Nottiani, A. Cavazza, C. Sciancalepore, Poly (lactic acid) and its blends for packaging application: a review, Clean Technol. 5 (2023) 1304–1343, https://doi.org/10.3390/cleantechnol5040066.
[5] A. Etxabide, B. Young, P.J. Bremer, P.A. Kilmartin, Non-permanent primary food packaging materials assessment: identification, migration, toxicity, and consumption of substances, Compr. Rev. Food Sci. Food Saf. 21 (2022) 4130–4145, https://doi.org/10.1111/1541-4337.13001.
[6] A. Cavazza, M. Mattarozzi, A. Franzoni, M. Careri, A spotlight on analytical prospects in food allergens: from emerging allergens and novel foods to bioplastics and plant-based sustainable food contact materials, Food Chem. 388 (2022) 132951, https://doi.org/10.1016/j.foodchem.2022.132951.
[7] N. Riboni, F. Bianchi, A. Cavazza, M. Piergiovanni, M. Mattarozzi, M. Careri, Mass spectrometry-based techniques for the detection of non-intentionally added substances in bioplastics, Separations 10 (2023) 222, https://doi.org/10.3390/separations10040222.
[8] L. Zimmermann, A. Dombrowski, C. Völker, M. Wagner, Are bioplastics and plant-based materials safer than conventional plastics? In vitro toxicity and chemical composition, Environ. Int. 145 (2020) 106066, https://doi.org/10.1016/j.envint.2020.106066.
[9] European Union, Commission Regulation (EU) No 10/2011 of 14 January 2011, 2011. https://eur-lex.europa.eu/LexUriServ/LexUriServ.do?uri=OJ:L:2011:012:0001:0089:EN:PDF.
[10] C. Nerin, A.R. Boobis, K. Debarata, S. Dubail, T. Gude, C. Kirchnawy, B. Knaup, K. J. Korzeniowski, C. Lacourt, O. Vitrac, S. Wang, P.K.T. Oldring, Review of potential areas for global harmonization of risk assessment protocols for Food Contact Materials (FCMs), Trends Food Sci. Technol. 159 (2025) 104987, https://doi.org/10.1016/j.tifs.2025.104987.
[11] V.García Ibarra, A. Rodríguez Bernaldo de Quirós, P. Paseiro Losada, R. Sendón, Non-target analysis of intentionally and non intentionally added substances from plastic packaging materials and their migration into food simulants, Food Packag. Shelf Life. 21 (2019) 100325, https://doi.org/10.1016/j.fpsl.2019.100325.
[12] P. Vázquez-Loureiro, R. Cariou, G. Dervilly, B. Le Bizec, A. Lestido-Cardama, L. Barbosa-Pereira, R. Sendón, J. Bustos, A. Gasco, P. Paseiro-Losada, A. Rodríguez Bernaldo de Quirós, Identification of volatile and semi-volatile components in food contact bioplastics based on GC–MS non-targeted screening, J. Chromatogr. A. 1762 (2025) 466377, https://doi.org/10.1016/j.chroma.2025.466377.
[13] B. Caux, C. De Saint Jores, R. Abou-Naccoul, C. West, From extraction to detection: an analytical journey of plastic additives and their migrations, TrAC Trends Anal. Chem. 191 (2025) 118373, https://doi.org/10.1016/j.trac.2025.118373.
[14] F. Akoueson, I. Paul-Pont, K. Tallec, A. Huvet, P. Doyen, A. Dehaut, G. Duflos, Additives in polypropylene and polylactic acid food packaging: chemical analysis and bioassays provide complementary tools for risk assessment, Sci. Total Environ. 857 (2023) 159318, https://doi.org/10.1016/j.scitotenv.2022.159318.
[15] O. Pitirollo, M. Grimaldi, E. Messinese, M. Fontanarosa, M. Mattarozzi, A. Cavazza, Evaluation of Possible Contaminants from Sustainable Materials Intended for Food Contact, Sustainability 17 (2024) 178, https://doi.org/10.3390/su17010178.
[16] Z. Tian, S.-K. Kim, K. Kim, Distinguishing between extractable and leachable contents of styrene oligomers in various polystyrene consumer products: towards environmentally realistic scenarios, J. Hazard. Mater. 487 (2025) 137190, https://doi.org/10.1016/j.jhazmat.2025.137190.
[17] K. Savva, X. Borrell, T. Moreno, I. Pérez-Pomeda, C. Barata, M. Llorca, M. Farré, Cytotoxicity assessment and suspected screening of PLASTIC ADDITIVES in bioplastics of single-use household items, Chemosphere 313 (2023) 137494, https://doi.org/10.1016/j.chemosphere.2022.137494.
[18] E. Omer, A. Bakiri, Y.-A. Hammel, M.J. Sanders, S. Koster, O. Ciclet, Deciphering the complexity of the chemicals in food packaging materials using molecular networks, Food Chem. 462 (2025) 140853, https://doi.org/10.1016/j.foodchem.2024.140853.
[19] M. Aznar, S. Ubeda, N. Dreolin, C. Nerín, Determination of non-volatile components of a biodegradable food packaging material based on polyester and polylactic acid (PLA) and its migration to food simulants, J. Chromatogr. A. 1583 (2019) 1–8, https://doi.org/10.1016/j.chroma.2018.10.055.
[20] A. Gałuszka, Z. Migaszewski, J. Namieśnik, The 12 principles of green analytical chemistry and the SIGNIFICANCE mnemonic of green analytical practices, TrAC - Trends Anal. Chem. 50 (2013) 78–84, https://doi.org/10.1016/j.trac.2013.04.010.
[21] R.O. Martins, C. Will, M.F.A. Magalhães, F.M. Lanças, Advances in miniaturized liquid sample preparation techniques for environmental analysis: a special look towards green solvents and automation, J. Chromatogr. Open. 8 (2025) 100240, https://doi.org/10.1016/j.jcoa.2025.100240.
[22] A. Özgür, E.Z. Aktürk, D. Köseoğlu, C. Onac, A. Akdoğan, Deep Eutectic Solvent-based green extraction and gas chromatography determination of phthalates released from food contact materials, J. Food Compos. Anal. 118 (2023) 105208, https://doi.org/10.1016/j.jfca.2023.105208.
[23] E. Rodríguez-Rodríguez, C. Herrero-Lodares, M. Sánchez-Prieto, B. Olmedilla-Alonso, C. Sánchez-Moreno, B. de Ancos, Sustainable extraction methods of carotenoids from mango (Mangifera indica L. 'Kent') pulp: ultrasound assisted extraction and green solvents, Food Chem 450 (2024) 139253, https://doi.org/10.1016/j.foodchem.2024.139253.
[24] N. Yabueng, S.C. Napathorn, Toward non-toxic and simple recovery process of poly (3-hydroxybutyrate) using the green solvent 1,3-dioxolane, Process Biochem. 69 (2018) 197–207, https://doi.org/10.1016/j.procbio.2018.02.025.
[25] M. Melchiorre, P.H.M. Budzelaar, M.E. Cucciolito, R. Esposito, E. Santagata, F. Ruffo, 1,3-Dioxolane compounds (DOXs) as biobased reaction media, Green Chem. 25 (2023) 2790–2799, https://doi.org/10.1039/D3GC00227F.
[26] C.-W. Cho, T.P.T. Pham, Y. Zhao, S. Stolte, Y.-S. Yun, Review of the toxic effects of ionic liquids, Sci. Total Environ. 786 (2021) 147309, https://doi.org/10.1016/j.scitotenv.2021.147309.
[27] D.T. Xuan, H.M.T. Nguyen, V.D. Hoang, Recent applications of analytical quality-by-design methodology for chromatographic analysis: a review, Chemom. Intell. Lab. Syst. 254 (2024) 105243, https://doi.org/10.1016/j.chemolab.2024.105243.
[28] R. Deidda, S. Orlandini, P. Hubert, C. Hubert, Risk-based approach for method development in pharmaceutical quality control context: a critical review, J. Pharm. Biomed. Anal. 161 (2018) 110–121, https://doi.org/10.1016/j.jpba.2018.07.050.
[29] E. Lorre, N. Riboni, F. Bianchi, S. Orlandini, S. Furlanetto, M. Careri, M. Zilius, Quality by design in the optimization of the ultrasonic assisted solvent extraction for the GC-MS determination of plasticizers in sediments and shells, Talanta Open 8 (2023) 100258, https://doi.org/10.1016/j.talo.2023.100258.
[30] C. Ancillotti, S. Orlandini, L. Ciofi, B. Pasquini, C. Caprini, C. Droandi, S. Furlanetto, M. Del Bubba, Quality by design compliant strategy for the development of a liquid chromatography–tandem mass spectrometry method for the determination of selected polyphenols in Diospyros kaki, J. Chromatogr. A. 1569 (2018) 79–90, https://doi.org/10.1016/j.chroma.2018.07.046.
[31] F. Bianchi, F. Fornari, N. Riboni, C. Spadini, C.S. Cabassi, M. Iannarelli, C. Carraro, P.P. Mazzeo, A. Bacchi, S. Orlandini, S. Furlanetto, M. Careri, Development of novel cocrystal-based active food packaging by a Quality by Design approach, Food Chem. 347 (2021) 129051, https://doi.org/10.1016/j.foodchem.2021.129051.
[32] M. Piergiovanni, V. Termopoli, C. Maffezzoni, N. Riboni, V. Consonni, F. Bianchi, M. Mattarozzi, D. Ballabio, M. Careri, Condensed phase membrane introduction mass spectrometry: a new frontier for the real-time monitoring of hazardous chemical migration from food contact materials, Green Anal. Chem. 12 (2025) 100199, https://doi.org/10.1016/j.greeac.2024.100199.
[33] F. Pena-Pereira, W. Wojnowski, M. Tobiszewski, AGREE—analytical GREEnness metric approach and software, Anal. Chem. 92 (2020) 10076–10082, https://doi.org/10.1021/acs.analchem.0c01887.
[34] M. Tobiszewski, J. Namieśnik, Scoring of solvents used in analytical laboratories by their toxicological and exposure hazards, Ecotoxicol. Environ. Saf. 120 (2015) 169–173, https://doi.org/10.1016/j.ecoenv.2015.05.043.
[35] N. Manousi, W. Wojnowski, J. Płotka-Wasylka, V. Samanidou, Blue applicability grade index (BAGI) and software: a new tool for the evaluation of method practicality, Green Chem. 25 (2023) 7598–7604, https://doi.org/10.1039/D3GC02347H.
[36] B. Ma, X. Wang, Y. He, Z. Dong, X. Zhang, X. Chen, T. Liu, Effect of poly(lactic acid) crystallization on its mechanical and heat resistance performances, Polymer (Guildf) 212 (2021) 123280, https://doi.org/10.1016/j.polymer.2020.123280.
[37] G.F. Schirinzi, M. Llorca, R. Seró, E. Moyano, D. Barceló, E. Abad, M. Farré, Trace analysis of polystyrene microplastics in natural waters, Chemosphere 236 (2019) 124321, https://doi.org/10.1016/j.chemosphere.2019.07.052.

[38] M.Á. Herrador, A.G. Asuero, A.G. González, Estimation of the uncertainty of indirect measurements from the propagation of distributions by using the Monte-Carlo method: an overview, Chemom. Intell. Lab. Syst. 79 (2005) 115–122, https://doi.org/10.1016/j.chemolab.2005.04.010.
[39] F. Bianchi, M. Careri, A. Mangia, M. Musci, Retention indices in the analysis of food aroma volatile compounds in temperature-programmed gas chromatography: database creation and evaluation of precision and robustness, J. Sep. Sci. 30 (2007) 563–572, https://doi.org/10.1002/jssc.200600393.
[40] N. Riboni, E. Ribezzi, E. Marraffa, P. Mora, C. Bellucci, F. Bianchi, M. Careri, An ex vivo headspace gas chromatography-mass spectrometry method for the determination of short-chain siloxanes in silicon oil tamponades used in ophthalmic surgery, J. Pharm. Biomed. Anal. 238 (2024) 115871, https://doi.org/10.1016/j.jpba.2023.115871.
[41] M.B. Swanson, G.A. Davis, L.E. Kincaid, T.W. Schultz, J.E. Bartmess, S.L. Jones, E. Lou George, A screening method for ranking and scoring chemicals by potential human health and environmental impacts, Environ. Toxicol. Chem. 16 (1997) 372–383, https://doi.org/10.1002/etc.5620160237.
[42] J. Ostrowska, W. Sadurski, M. Paluch, P. Tyński, J. Bogusz, The effect of poly (butylene succinate) content on the structure and thermal and mechanical properties of its blends with polylactide, Polym. Int. 68 (2019) 1271–1279, https://doi.org/10.1002/pi.5814.
[43] Y. Cai, J. Lv, J. Feng, Spectral characterization of four kinds of biodegradable plastics: poly (Lactic Acid), Poly (Butylenes Adipate-Co-Terephthalate), Poly (Hydroxybutyrate-Co-Hydroxyvalerate) and Poly (Butylenes Succinate) with FTIR and Raman Spectroscopy, J. Polym. Environ 21 (2013) 108–114, https://doi.org/10.1007/s10924-012-0534-2.
[44] S. Ubeda, M. Aznar, C. Nerín, Determination of volatile compounds and their sensory impact in a biopolymer based on polylactic acid (PLA) and polyester, Food Chem. 294 (2019) 171–178, https://doi.org/10.1016/j.foodchem.2019.05.069.
[45] E. López Sanvicente, L. Barbosa-Pereira, R. Sendón, A. Rodríguez Bernaldo de Quirós, A. Lestido-Cardama, Identification of potential migrants in food contact materials labeled as bio-based and/or biodegradable by GC-MS, Coatings 15 (2025) 751, https://doi.org/10.3390/coatings15070751.
[46] P. Harmon, R. Otter, A review of common non-ortho-phthalate plasticizers for use in food contact materials, Food Chem. Toxicol. 164 (2022) 112984, https://doi.org/10.1016/j.fct.2022.112984.
[47] I. Coralli, A.G. Rombolà, D. Fabbri, Analytical pyrolysis of the bioplastic PBAT poly (butylene adipate-co-terephthalate), J. Anal. Appl. Pyrolysis. 181 (2024) 106577, https://doi.org/10.1016/j.jaap.2024.106577.
[48] E. Canellas, P. Vera, C. Nerín, UPLC–ESI-Q-TOF-MSE and GC–MS identification and quantification of non-intentionally added substances coming from biodegradable food packaging, Anal. Bioanal. Chem. 407 (2015) 6781–6790, https://doi.org/10.1007/s00216-015-8848-2.
[49] E.D. Tsochatzis, J. Alberto Lopes, E. Hoekstra, H. Emons, Development and validation of a multi-analyte GC-MS method for the determination of 84 substances from plastic food contact materials, Anal. Bioanal. Chem. 412 (2020) 5419–5434, https://doi.org/10.1007/s00216-020-02758-7.
[50] S. Saeidlou, M.A. Huneault, H. Li, C.B. Park, Poly(lactic acid) crystallization, Prog. Polym. Sci. 37 (2012) 1657–1677, https://doi.org/10.1016/j.progpolymsci.2012.07.005.
[51] C. Lambré, J.M. Barat Baviera, C. Bolognesi, A. Chesson, P.S. Cocconcelli, R. Crebelli, D.M. Gott, K. Grob, E. Lampi, M. Mengelers, A. Mortensen, I. Steffensen, C. Tlustos, H. Van Loveren, L. Vernis, H. Zorn, L. Castle, E. Di Consiglio, R. Franz, M.R. Milana, E. Barthélémy, D. Comandella, G. Rivière, Safety assessment of the substance 'phosphorous acid, triphenyl ester, polymer with 1,4-cyclohexanedimethanol and polypropylene glycol, C10–16 alkyl esters', for use in food contact materials, EFSA J. 22 (2024) e8694, https://doi.org/10.2903/j.efsa.2024.8694.
[52] X. Meng, G. Shi, C. Wu, W. Chen, Z. Xin, Y. Shi, Y. Sheng, Chain extension and oxidation stabilization of Triphenyl Phosphite (TPP) in PLA, Polym. Degrad. Stab. 124 (2016) 112–118, https://doi.org/10.1016/j.polymdegradstab.2015.12.003.
[53] S. Hazer, M. Coban, A. Aytac, Effects of ammonium polyphosphate and triphenyl phosphate on the flame retardancy, thermal, and mechanical properties of glass fiber–reinforced PLA/PC composites, Fire Mater. 43 (2019) 277–282, https://doi.org/10.1002/fam.2696.
[54] A. Remezov, B. Knaup, S. Wermann, D. Marchesi, F. Rüttler, W. Vetter, Factors influencing migration of NIAS: model experiments with 7,9-di-tert-butyl-1-oxas-piro(4,5)deca-6,9-diene-2,8-dione (Arvin 8), Food Packag. Shelf Life 48 (2025) 101453, https://doi.org/10.1016/j.fpsl.2025.101453.
[55] M. Rani, W.J. Shim, G.M. Han, M. Jang, N.A. Al-Odaini, Y.K. Song, S.H. Hong, Qualitative analysis of additives in plastic marine debris and its new products, Arch. Environ. Contam. Toxicol. 69 (2015) 352–366, https://doi.org/10.1007/s00244-015-0224-x.
[56] H. Li, L. Chen, X. Wu, S. Wu, Q. Su, B. Dong, D. Li, T. Ma, H. Zhong, X. Wang, J. Zheng, C. Nerín, Characterization of volatile organic compounds in food contact paperboards and elucidation of their potential origins from the perspective of the raw materials, Food Packag. Shelf Life. 37 (2023) 101062, https://doi.org/10.1016/j.fpsl.2023.101062.
[57] D. Ballabio, F. Grisoni, R. Todeschini, Multivariate comparison of classification performance measures, Chemom. Intell. Lab. Syst. 174 (2018) 33–44, https://doi.org/10.1016/j.chemolab.2017.12.004.