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Special Guest Editor article

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FraMiTrACR: A Sustainable and Economical Technology for Analytical Sample Preparation

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Abstract

Background: There are several globally recognized methods for preparing laboratory samples. Of these, the Quick, Easy, Cheap, Effective, Rugged and Safe (QuEChERS) and Quick Polar Pesticides (QuPPe) methods are commonly used for food laboratory sample preparation. As an alternative, we developed a fractionation method using Fractionation of Milk for Trace Analysis of Contaminats and Residues (FraMiTrACR).

Objective: We present a life-cycle assessment for the QuEChERS, QuPPe, and FraMiTrACR methods. Our objective was to collect data to evaluate the carbon footprint of each method. However, as the ecological factors alone do not inform suitability of any given method, we also evaluated economic factors.

Methods: Our life cycle assessments (LCAs) followed ISO 14040/44 to determine the carbon footprint of each method. Also, we have analyzed existing data to support our comparison of all three methods.

Results: The mass of consumables and packaging for our FraMiTrACR method was observed to decrease by 45 and 34% from those required for the QuPPe and QuEChERS methods, respectively. Furthermore, we calculated a 43% reduction in carbon footprint when using FraMiTrACR compared to QuPPe and a 31% reduction compared to QuEChERS. In addition, we determined that our method offers time savings >87 and >71% compared to QuEChERS and QuPPe, respectively. The main economic benefit of FraMiTrACR comes from 84 and 70% labor cost savings compared to QuEChERS and QuPPe, respectively. The laboratory using the fractionation method can process 320 samples with FraMiTrACR within 8 h, an 87% increase in potential compared to QuEChERS and a 71% increase compared to QuPPe.

Conclusion: Fractionation using FraMiTrACR is a more sustainable method for analytical sample preparation, offering the same quality of results and far-reaching economic advantages.

Highlights: In comparison, FraMiTrACR uses up to 45% less consumables and packaging by weight and a reduction in kg CO_2eq of up to 43%. In addition, the fractionation method offers up to 85% time-saving and up to an 84% reduction in labor cost per sample.

Recognized test methods for the determination of residues and contaminants in food samples usually consist of a residue-specific laboratory sample preparation process followed by chromatography-based analysis (1, 2). There are many laboratory sample preparation methods worldwide, but two are particularly well-known in Europe. One is the "Quick, Easy, Cheap, Effective, Rugged and Safe" (QuEChERS) method, and the other is the "Quick Polar Pesticides" (QuPPe) method (3). The aim of this study was to compare these methods with a novel fractionation method in terms of environmental, technical, and economic aspects. The three methods are compared in Figure 1, which provides an overview of the process steps, and the consumable and energy requirements.

QuEChERS

The QuEChERS method was introduced in 2003 as a versatile approach for the determination of pesticides in fruit and vegetables (4). The method is very suitable for processing substances that have non-polar or moderate polar properties. It consists of several steps as follows using milk as an example: 10 mL acetonitrile (ACN) is added to a 4 mL milk sample, which is homogenized and then mixed for 10 s using a vortex mixer and a further 5 min using a mechanical shaker. The laboratory sample is then centrifuged for 10 min, the supernatant is collected, and 500 mg octadecyl sorbent (C18CE) is added. The treated laboratory sample is mixed by a vortex mixer for 10 s, shaken by a mechanical shaker for another 1 min, and centrifuged again for 5 min. The final 10 mL supernatant is transferred to a weighed glass tube and concentrated to a weight of 1 g by evaporation under vacuum at 40°C for 2–3 h. Finally, 750 µL water and 250 µL ACN are added, and the extract is filtered through a 0.45 µm syringe filter before LC–MS/MS analysis (Figure 1).

QuPPe

To close the technical gap for highly polar pesticides (which cannot be determined by the QuEChERS method), the QuPPe method

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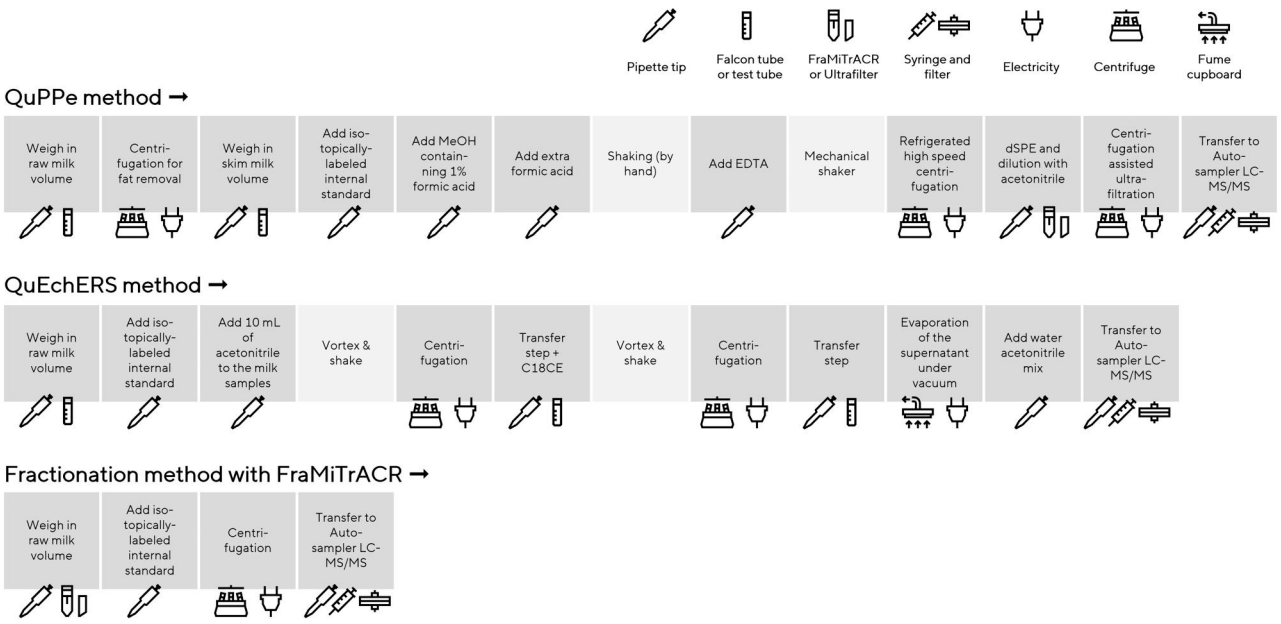

Figure 1. Comparison of the process steps and consumables used for the QuPPe, QuEChERS, and FraMiTrACR sample preparation methods.

was published by the European Reference Laboratory for Pesticides Requiring Single Determination Methods (EURL-SRM) in 2008 (5). This method has been available since 2013 for laboratory samples of both plant and animal origin (6). The QuPPe method requires several steps for laboratory sample preparation. Taking milk sample preparation as an example, fat is removed from the raw milk by centrifugation. Alternatively, the whole milk, which is homogenized beforehand, is diluted by adding 0.5 mL water to the 10 g milk sample. The resulting laboratory sample is treated with 10 mL acidified methanol and 100 µL formic acid, then 1 mL EDTA is added. This breaks down the protein, chelates metal ions, and extracts the analytes. After a second centrifugation step, the 2 mL raw extract is treated with 2 mL acetonitrile and 100 mg adsorbent and centrifuged again. The resulting supernatant is then transferred to a centrifugal filter for a final clarification step prior to laboratory sample analysis (5–7).

Fractionation Method by FraMiTrACR

In contrast to the multi-step laboratory sample preparation methods described above, our fractionation method is a one-step process. The method is based on the development of a fractionation unit "Fractionation of Milk for Trace Analysis of Contaminants and Residues" (FraMiTrACR), which makes it possible to separate complex laboratory sample matrixes in a single step, passively and without using additives or cleanup procedures, and to use the aqueous fraction directly for further analysis (1, 2). In previous publications, we have used fat-containing, non-homogenized raw milk as a laboratory sample representing a matrix that is usually challenging to process. The raw milk was dispensed into a FraMiTrACR unit and after a centrifugation time of 15 min, the filtrate was used directly for chromatographic analysis. This extract gave comparable results to laboratory samples prepared by QuEChERS and QuPPe methods.

Life Cycle Assessment/Environmental Sustainability Assessment of Laboratory Sample Preparation

Life cycle assessment (LCA) is an established method to determine the environmental impact of technical systems. Its underlying premise is to account for all material and energy flows connected to the system under study while investigating the entire life cycle—from extraction of raw materials to manufacturing, logistics, product use, and end-of-life. Based on this holistic analysis, the systems under study can be assessed for their environmental impact, e.g., carbon footprint. LAC gains importance across various industries as a quantitative tool that enables decision-making. It is especially applicable to the laboratory industry when introducing environmentally sustainable practices and new laboratory technologies. Different aspects may be addressed, such as the reduction of plastic consumables, increased energy efficiency, or improved circularity, all of which contribute to decarbonization of laboratory operations. Several studies have been carried out to assess the environmental impact of different laboratory sample preparation methods. For example, Farley et al. have discussed the carbon footprint advantages of reusable versus single-use plastic consumables (8). In a 2022 study, Raccary et al. compared the environmental impacts of stir bar sorptive extraction (SBSE) and solid-phase extraction (SPE), laying the methodological foundations for comparative LCA of laboratory sample preparation methods (9). Their study suggested that energy, laboratory equipment, solvents, gases, transport, and waste treatments should all be considered within LCA. Finally, González-Martín et al. have proposed a semi-quantitative metric to evaluate the sustainability of laboratory sample preparation methods (10). This combines criteria of extractants, procedural efficiency, energy consumption, waste, and reusability into a score that can be applied to decision-making. The present study follows the structure of an LCA according to ISO 14040/44, including goal and scope, life cycle inventory, life cycle impact assessment, and interpretation with the intention to compare the QuEChERS, QuPPe, and FraMiTrACR methods based on the required consumables and resulting carbon emissions. Currently, there is no specific guidance for performing LCAs or carbon footprint studies for test methods, e.g., product category rules (11). However, we considered system elements proposed within the recent literature when defining the scope of our study (9, 10). Modeling choices, data acquisition methods, and further assumptions are described in detail below.

Experimental

LCA—Goal and Scope

The goal of the LCA is the comparison of the carbon footprint of the QuEChERS, QuPPe, and FraMiTrACR methods based on the preparation of 16 laboratory samples. As illustrated in Figure 1, the major differences between these methods lie in the quantity and characteristics of the required consumables, the electricity demands of benchtop processes (mainly centrifugation), and the use of chemicals. Therefore, quantification of these aspects formed the foundation of our study, and this is discussed specifically in *LCA—Life Cycle Inventory*. Because our assessment was intended to illustrate a representative scenario at an average European testing institute, we defined a set of assumptions. The required consumables (pipette tips, tubes, syringes, syringe filters, etc.) should be representative of a typical situation in a European laboratory and should not represent one specific manufacturer of consumables. Therefore, consumable manufacturing was assumed to take place in the United Kingdom, using raw materials from suppliers with 1000 km of upstream transport distance to the production facility, an average electricity mix, and an average shipping distance to customers of 1000 km. Consumable end-of-life was assumed to be incineration with energy recovery. End-of-life shares between incineration, recycling, and landfill for consumable packaging were determined based on average market statistics.

The impact assessment method was enviromental footprint (EF) 3.1 Climate Change, fossil. Details on system boundaries, limitations, and cutoffs are described in *LCA—Life Cycle Inventory*.

LCA—Life Cycle Inventory

To model the foreground system of the life cycle inventory (LCI), the weight of the consumables and packaging and the electricity demand was determined for each method. Primary data collection for consumable and packaging weights was carried out at Sartorius (Göttingen, Germany). Figure 2 and Table 1 show the respective weights of the consumables required for each method when preparing 16 laboratory samples. Data were collected by weighing sample consumables from different manufacturers and reviewing manufacturer specifications for material composition. Scaling for missing sizes was applied when data for a specific size was not available. Glass test tubes used in the QuEChERS method were assumed to have 20 use cycles with intermediate cleaning and autoclaving steps.

The QuPPe method requires 1.95 kg of consumables and packaging, the QuEChERS method 1.61 kg, and fractionation by FraMiTrACR only 1.07 kg. The dominant materials are polypropylene (PP, for all consumables including pipette tips, centrifuge tubes, syringes, and syringe filters), polycarbonate (PC, for FraMiTrACR) and high-density polyethylene (HDPE, for centrifuge tube lids). For packaging, materials included PP for pipette tip boxes, low-density polyethylene (LDPE) for packaging films, and cardboard.

Primary data collection to determine electricity consumption was also carried out at Sartorius. Representative test runs of a benchtop centrifuge were metered, while the electricity demand of fume cupboards used in the QuEChERS method was calculated using the device-connected power data related to the time in use. During our assessment, it was decided that the energy demand of vortex and mechanical mixers was negligible, and therefore this is not included in our calculation. An overview of electricity demands is given in Table 2. Solvent and sorbent consumption is also listed for the QuEChERS and QuPPe methods in Table 2.

The LCA model was created using Sphera LCAFE software with the Sphera 2023.2 database as well as the Ecoinvent 3.8 database. Background data sets taken from those databases include polymer materials for the consumables and packaging (PP, LDPE, HDPE, PC, and cardboard) as well as manufacturing processes for injection molding and film manufacturing, electricity mixes for manufacturing and product use, transport processes for upstream transport and distribution, and the datas ets to model the incineration and landfill processes for end-of-life. Table 3 shows the selection of the different data sets from the databases. Similarly, data for sterilization of consumables and autoclaving and washing of glass test tubes for QuEChERS was approximated from data available at Sartorius. The contributions are included in the manufacturing stage for consumables. Regarding solvents, the data set for acetonitrile was taken from the Sphera 2023.2 database, while data sets for methanol, formic acid, and EDTA were applied from Ecoinvent 3.8. Packaging and upstream transport of solvents was not included in the model due to its minor impact. Sorbents used in the QuEChERS and QuPPe methods could not be included in the model due to missing information on their environmental impact factors.

The end-of-life quota for packaging has been modeled based on average data from Eurostat from 2021, assuming 40.7% recycling, 37% incineration with energy recovery, and 22.3% landfill for the share of plastic materials in packaging, and 82.5%

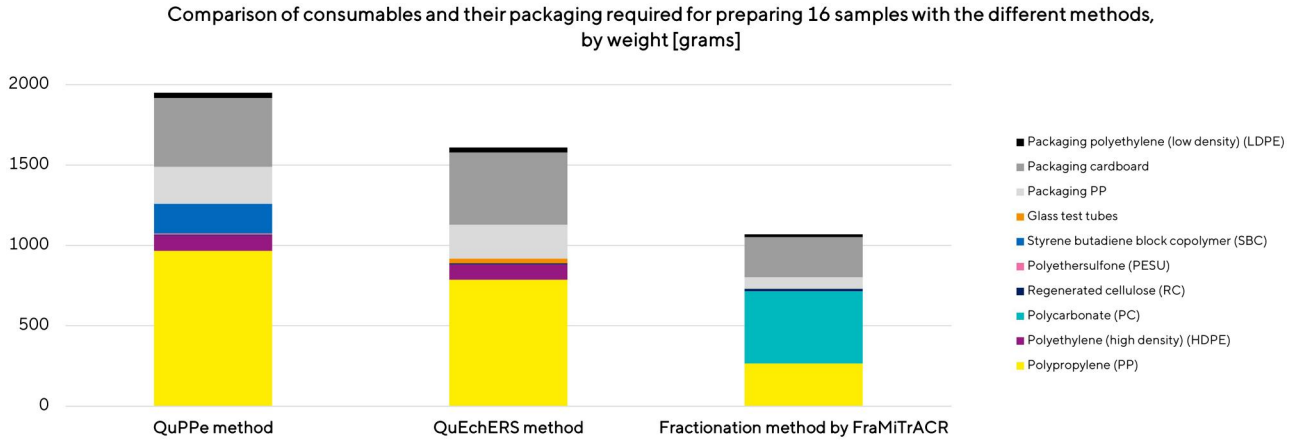

Figure 2. Comparison of the consumables required to prepare 16 samples by the QuPPe, QuEChERS, and FraMiTrACR methods, and their packaging, by weight in grams.

Table 1. Mass of the consumables and packaging required for 16 samples per method, as assessed by weighing representative consumables and scaling for missing sizes

Material description	QuPPe method consumables mass, g	QuEChERS consumables mass, g	FraMiTrACR consumables mass, g
PP (polypropylene)	966	787	266
HDPE (high-density polyethylene)	94	94	0
PC (polycarbonate)	0	0	448
Membrane material	16	8	17
SBC (styrene-butadiene block copolymer)	184	0	0
Glass test tubes	0	30	0
Packaging PP	229	210	72
Packaging cardboard	429	449	250
Packaging LDPE (low-density polyethylene)	33	33	18
Sum	1950	1610	1069

Table 2. Comparisons of preparation time per sample, electricity demand, solvent consumption, and labor cost per sample

Material description	QuPPe method	QuEChERS method	FraMiTrACR method
		Preparation time for 16 samples	
Total working time, min	83	180	24
Active working time, min	28	30	9
Passive working time, min	55	150	15
		Electricity demand for 16 samples	
Electricity demand, kWh	1.7	5.63	0.27
		Solvent and sorbent volumes used for 16 samples	
Total volume, mL	~172	~197	0
Acetonitrile, mL	164	32	0
Methanol with formic acid, mL	0	160	0
Formic acid, mL	0	1.6	0
10% EDTA solution, mL	0	16	0
QuEChERS sorbent CE18C, mg	8000	0	0
QuPPe C18 sorbent, mg	0	1600	0
		Labor costs for 16 samples	
Total labor costs, €	37.00	70.00	11.00
Active working time labor costs, € (40€/h)	18.67	20.00	6.00
Passive working time labor costs, € (20€/h)	18.33	50.00	5.00

recycling, 8.2% incineration with energy recovery, and 9.3% landfill for the cardboard shares. Recycling shares of the consumables packaging were modeled using a cutoff approach.

LCA—Impact Assessment

As a further part of our LCA, we calculated the greenhouse gas emissions for each method, using the impact assessment method EF 3.1 Climate Change, fossil. This metric was chosen because the reduction of fossil carbon emissions from industrial processes is the focus of this indicator. Figure 3 and Table 4 show the values determined for consumables manufacturing, upstream transport, packaging manufacturing, distribution, electricity, solvents, consumables incineration, and packaging end-of-life. Consumables manufacturing, and incineration are major contributors to the environmental impact of all three methods. This can be linked to the consumable requirements summarized in Figure 2, with QuPPe using the highest number of consumables. However, the benefit by weight for the FraMiTrACR method is partly compensated by use of PC in consumables, compared to the other methods that use a larger share of PP consumables. Packaging manufacturing and end-of-life for consumables directly relate to the number of consumables used for each of the methods. Electricity demand is also a major contributor to the environmental impact. Here, QuEChERS has the largest impact due to the vacuum evaporation step. The impact from electricity consumption for QuPPe and FraMiTrACR is related to centrifugation, and the lower number of centrifugal steps for FraMiTrACR results in our method having the lowest impact. Solvents account for almost 10% of carbon emissions for QuPPe, due in particular to the use of acetonitrile, while FraMiTrACR does not have any carbon emissions in this category because solvents are not required for this method.

In summary, fractionation by FraMiTrACR leads to lower carbon emissions compared to QuPPe and QuEChERS, due to the lower number of consumables used, fewer centrifugation steps, and the absence of solvents in this method.

Preparation Time Per Laboratory Sample Run Related to Electricity, Solvents and Labor Costs

In two previous studies, we used the preparation of raw milk samples in the laboratory as a model to compare our fractionation method with QuPPe for the determination of chlorate and perchlorate and with QuEChERS for the determination of antibiotic residues (12). In both publications, a significant reduction in laboratory sample preparation time was evident when using FraMiTrACR. We used the laboratory sample preparation times from our previous studies to evaluate the labor costs for each method. The preparation time was divided between active and

Table 3. Background data sets applied for the Life Cycle Assessment model

Activity	Database	Background data set applied
Consumables manufacturing		
Polypropylene	Sphera 2023.2	DE[a]: Polypropylene granulate
High-density polyethylene	Sphera 2023.2	DE: Polyethylene high density granulate
Polycarbonate	Sphera 2023.2	DE: Polycarbonate granulate
Styrene-butadiene rubber	Sphera 2023.2	DE: Styrene-butadiene rubber
Glass test tubes	Sphera 2023.2	RER[b]: Borosilicate glass production
Injection moulding	Sphera 2023.2	GLO[c]: Plastic injection moulding (parameterized)
Electricity	Sphera 2023.2	GB[d]: Electricity grid mix
Upstream transport		
Road transport	Sphera 2023.2	GLO: Truck, Euro 0—6 mix, 20—26t gross weight/17.3t payload capacity
Diesel	Sphera 2023.2	RER: Diesel mix at filling station
Solvents		
Acetonitrile	Sphera 2023.2	DE: Acetonitrile
Methanol	Ecoinvent 3.8	GLO: market for methanol
Formic acid	Ecoinvent 3.8	RER: market for formic acid
EDTA	Ecoinvent 3.8	GLO: market for EDTA
Packaging manufacturing		
Packaging PP (polypropylene)	Sphera 2023.2	DE: Polypropylene granulate (PP)
Injection moulding	Sphera 2023.2	GLO: Plastic injection moulding (parameterized)
Electricity	Sphera 2023.2	GB: Electricity grid mix
Packaging cardboard	Sphera 2023.2	RER: Corrugated board 2018; excl.[e] paper production; input: paper Sphera/FEFCO[f]
Packaging cardboard	Sphera 2023.2	RER: Kraftliner 2018; by-products: tall oil, turpentine; cutoff EoL[g]; [mass allocation] Sphera/FEFCO
Packaging LDPE (low-density polyethylene)	Sphera 2023.2	DE: Polyethylene film (PE-LD[h]) without additives
Distribution		
Road transport	Sphera 2023.2	GLO: Truck, Euro 0–6 mix, 20–26t gross weight/17.3t payload capacity
Diesel	Sphera 2023.2	RER: Diesel mix at filling station
Centrifugation, fume cupboard, washing, and autoclaving		
Electricity	Sphera 2023.2	RER: Electricity grid mix
Consumables incineration		
Polypropylene (PP) incineration	Sphera 2023.2	RER: Polypropylene (PP) in waste incineration plant
Polyethylene (PE) incineration	Sphera 2023.2	RER: Polyethylene (PE) in waste incineration plant
Polycarbonate (PC) incineration	Sphera 2023.2	Polycarbonate (PC) in waste incineration plant
Other plastics incineration	Sphera 2023.2	DE: Plastic packaging in waste incineration plant
Consumables—credits for incineration	Sphera 2023.2	GLO: Electricity credit
Consumables—credits for incineration	Sphera 2023.2	GLO: Credit thermal energy
Packaging end-of-life		
Plastic packaging—landfill share (22.3%)	Sphera 2023.2	RER: Plastic waste on landfill Sphera
Plastic packaging—incineration share (37%)	Sphera 2023.2	DE: Plastic packaging in waste incineration plant
Plastic packaging—rredits for incineration	Sphera 2023.2	GLO: Electricity credit
Plastic packaging—credits for incineration	Sphera 2023.2	GLO: Credit thermal energy
Paper and cardboard—incineration share (8.2%)	Sphera 2023.2	Waste incineration of paper fraction in municipal solid waste (MSW)
Paper and cardboard—landfill share (9.3%)	Sphera 2023.2	RER: Paper waste on landfill

[a] DE = Germany.
[b] RER = Renewable energy ratio.
[c] GLO = Global.
[d] GB = Great Britain.
[e] Excl. = excluded.
[f] FEFCO = Fédération Européenne des Fabricants de Carton Ondule.
[g] EOL = End of Life.
[h] PE-LD = Polyethylene - Low Density.

passive working time for based on 16 laboratory samples. We chose 16 as the number of laboratory samples corresponding to one sample run, because this is the normal centrifuge tube capacity of a benchtop centrifuge and centrifugation is an integral part of all three methods. To calculate labor costs, we assumed an hourly wage of 40€ for active working time, during which a laboratory employee would be actively processing the laboratory samples, and half this hourly wage for passive working time, during which an employee can partially complete other tasks such as weighing laboratory samples until centrifugation-or evaporations steps are completed. The sum of the two calculated labor costs represents the total labor cost. In addition, we analyzed the consumption of solvents and sorbents for one sample run. The data are shown in Table 2. For the electricity demand, as mentioned above in the LCI, the data were collected using the specifications and operating time for each instrument used. Comparative measurements were also collected using electricity consumption meters connected to the electrical appliances.

Laboratory Sample Preparations

(a) *QuEChERS method*.—We described the working steps of the QuEChERS method detailed in the introduction. An illustration of the materials and working steps used can be seen in Figure 1. Further relevant information on the laboratory sample preparation procedure and the analysis can be found in the publication Steils et al. 2024 (1).

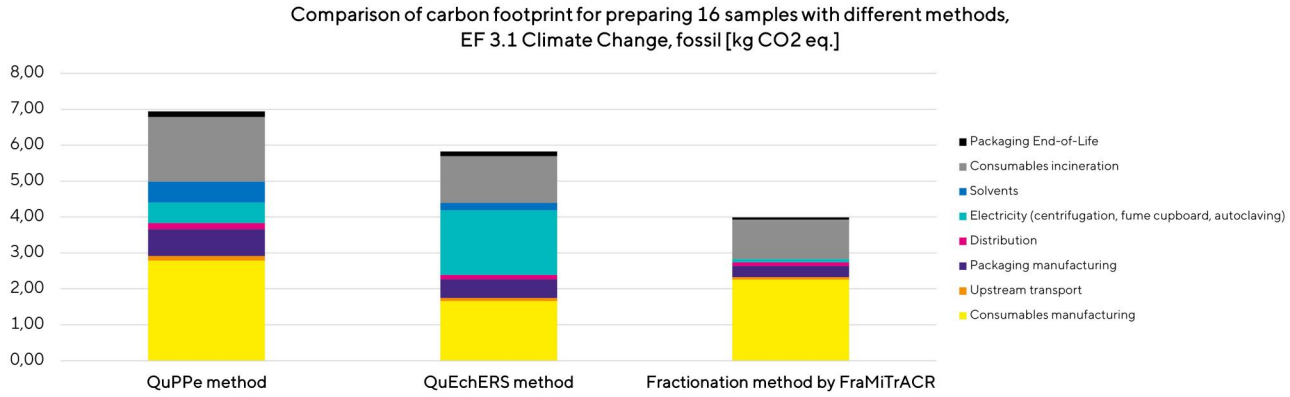

Figure 3. Comparison of the carbon footprint [kg CO_2 eq, EF 3.1 Climate Change, fossil] between the QuPPe, QuEChERS, and FraMiTrACR methods when preparing 16 samples.

Table 4. Calculation of the carbon footprint for processing 16 samples with each method (EF3.1 Climate Change, fossil)

Material description	QuPPe method, kg CO_2eq	QuEChERS method kg CO_2eq	FraMiTrACR method, kg CO_2eq
Consumables manufacturing	2.79	1.66	2.26
Upstream transport	0.13	0.08	0.07
Packaging manufacturing	0.74	0.52	0.32
Distribution	0.18	0.12	0.10
Electricity (centrifugation, fume cupboard, washing, autoclaving) – Electricity mix RER	0.57	1.80	0.09
Solvents	0.58	0.21	0
Consumables incineration	1.80	1.30	1.10
Packaging end-of-life	0.15	0.13	0.06
Sum	6.94	5.82	3.99

(b) *QuPPe method*.—We described the working steps of the QuPPe method detailed in the introduction. An illustration of the materials and working steps used can be seen in Figure 1. Further relevant information on the laboratory sample preparation procedure and the analysis can be found in the publication Steils et al. 2023 (2).

(c) *Fractionation method*.—We described the working steps of the fractionation method detailed in the introduction. An illustration of the materials and working steps used can be seen in Figure 1. Further relevant information on the laboratory sample preparation procedure and the analysis can be found in the publications (1, 2).

Sample Analysis by LC–MS/MS

Chromatographic separation and subsequent analysis of laboratory samples were carried out by ultra-high-pressure liquid chromatography (UHPLC) using a PerkinElmer LX50 UHPLC system and a QSight® 220 triple quadrupole tandem mass spectrometer. All instrument control, analysis, and data processing were performed using SimplicityTM 3Q software. Further relevant information on the laboratory sample preparation procedure and the analysis can be found in the publications (1, 2).

Comparison of the Analysis Results

We have previously compared our FraMiTrACR method in detail with the well-known QuPPe and QuEChERS methods in the publications (1, 2). Readers interested in additional details, such as LC parameters for the eluent gradient, can refer to the published data cited in ref. (12). In this study, our primary focus was to assess the sustainability of our novel method, with partial consideration of its economic impact. Therefore, results from our previous studies are not shown but are discussed alongside our findings on the carbon footprint of each method.

Results

Our goal was to perform a LCA for the QuPPe, QuEChERS, and FraMiTrACR methods to determine the possible environmental and economic advantages of our new fractionation method. We also aimed to relate the results of the LCA to other factors that are known to be important for analytical laboratories themselves, such as samples analyzed per day, storage capacity for consumables, disposal of materials and chemicals used, and efficient use of laboratory staff. For each of the three methods, we used a run of 16 samples to determine the weight of consumables and packaging, the electricity demand, the carbon footprint in kg CO_2eq, the total process time, the volume of solvents and sorbents used, and the labor costs. In addition, we referred to the analytical results from our previous studies to demonstrate the suitability of our new method for food testing laboratories with respect to its quantification and detection limits. The LCA for the consumables and packaging show an overall reduction in weight of 45% when using FraMiTrACR compared to QuPPe and 34% when compared to QuEChERS. Our fractionation method also shows advantages in terms of greenhouse gas emissions. Absolute reductions correspond to 43 and 31% savings on kg CO_2eq when comparing FraMiTrACR to QuPPe and QuEChERS, respectively. Furthermore, our method reduces electricity demand and working time due to the shorter overall process. Compared to QuPPe, the working time is reduced by 71% and the energy

Table 5. Summary of the overall reduction in consumable and packaging weight, carbon footprint, electricity demand, solvent consumption, and labor cost, when using the fractionation method with FraMiTrACR

Material description	QuPPe method	QuEChERS method	FraMiTrACR method
Sum of consumables and packaging weight, g	1950	1610	1069
Reduction, %, using fractionation	45	34	
Sum of kg CO_2eq	6.94	5.82	3.99
Reduction, %, using fractionation	43	31	
Total working time, min	83	180	24
Reduction, %, using fractionation	71	87	
Electricity demand, kWh	1.7	5.63	0.27
Reduction, %, by using fractionation	84	95	
Total solvent and sorbents volume, mL	172	197	0
Reduction, %, using fractionation	100	100	
Total labor costs, €	37.00	70.00	11.00
Reduction, %, using fractionation	70	84	

consumption by 84%. Compared to QuEChERS, working time is 87% shorter and uses 95% less energy. In addition, our fractionation method does not require the use of any solvents or sorbents. Finally, it also supports a reduction in labor costs by 70% compared to QuPPe and by 84% compared to QuEChERS. The data summarized above are shown in Table 5. Alongside the advantages determined by our LCA, previously collected analytical results relating to LODs and LOQs have demonstrated that our method using FraMiTrACR is sufficient for trace analysis of residues in food, at concentrations below the European maximum residue limit (MRL) (Table 6).

Discussion

Sustainability and environmental impact are new indicators that are being increasingly used for decision-making in the laboratory industry. Improvements in these areas are referred to as "green chemistry" and can be applied to the entire laboratory, including the technologies and laboratory sample preparation methods used. At least two approaches to increase sustainability and reduce environmental impact can be defined. One green chemistry approach aims to improve existing processes by, for example, using reduced quantities of solvents (12). The other approach aims to use less hazardous solvents and reagents and to ensure that the materials used are reusable or at least recyclable (10, 11). Furthermore, CO_2eq calculations or approximation methods have been described to compare the sustainability of laboratory sample preparation methods. Several recent publications advocate the use of defined standards for determining the sustainability of laboratory sample preparation methods and preparing LCAs (8–13).

The basic idea for the fractionation process is developed from the industrial application of membranes. For example, membranes are used specifically in the dairy industry or in the production of infant formula to remove proteins or salts from milk raw materials. These applications are the origin of the development of the fractionation method. During the development of our new method, we noticed two significant savings. The use of extraction agents, solvents, acids, and adsorbents is not necessary in the fractionation process. This reduction alone ensures an economic and ecological improvement for laboratories. In addition, no aids such as pipette tips and tubes are required to introduce the abovementioned substances into the actual laboratory sample. All in all, the fractionation method offers great economic and ecological advantages (12). The data is shown in Tables 1, 2, 4, and 5 and Figures 1–3. Our aim was therefore to prove that FraMiTrACR can reduce both consumable waste and the carbon footprint of analytical sample preparation, resulting in increased sustainability. We have compared our fractionation method with the current "gold standards" used to fulfill diverse analysis requirements, such as the QuEChERS and QuPPe methods (3–7). We determined that FraMiTrACR supports a large (34 or 45%) reduction in consumables and packaging, due to its single- versus multi-step process. In QuPPe and QuEChERS, new pipette tips or tubes must be used for each intermediate step, such as extraction and cleanup processes. In contrast, the FraMiTrACR fractionation approach was developed as a one-step method, such that only a small number of materials are needed. The data is shown in Figure 1–2, Table 1, and Table 2. This reduction in materials is also reflected in our calculations of greenhouse gas emissions, which are shown in Table 4 and Figure 3. The fractionation method with FraMiTrACR reduces carbon dioxide equivalent emissions by 43 % and 31 % respectively compared to QuPPe or QuEChERS. Table 2 shows fewer differences in the kg CO_2eq balance relating to materials production for the three methods. This can be explained by the fact that the FraMiTrACR unit is a more complex product than pipette tips or centrifuge tubes and therefore has a higher impact in this category. However, taking the larger number of consumables and packaging used in QuPPe and QuEChERS into account, it becomes clear that these methods generate higher total CO_2 emissions due to increased resource consumption.

The amount of electricity used is also a decisive factor in determining whether a process has a high impact on CO_2 emissions or not (Table 5). Here also, it can be said that laboratory sample preparation with FraMiTrACR offers the highest potential for analytical laboratories to save energy and reduce CO_2 emissions, therefore increasing the sustainability of their sample preparation processes. It should be mentioned that the QuEChERS and QuPPe methods use mechanical shakers or vortex mixers, which also require electricity, although this energy demand has not been included in our LCA, due to the relatively low power demands that we identified in our energy consumption measurements.

The use of solvents and sorbents will also increase CO_2 emissions, although sorbents were not accounted for in our LCA because supplier-specific emission factors were not available at the time of our investigation. However, considering that the QuEChERS and QuPPe methods use such substances and that our fractionation method deliberately avoids them, it can be assumed that there is an even greater CO_2 reduction than that shown in Tables 4 and 5 when using FraMiTrACR.

Table 6. Comparison of the LOD and LOQ between the QuEChERS, QuPPe, and analyte fractionation methods, in relation to the European MRL (1, 2, 14)

	Amoxicillin	Ampicillin	Cloxacillin
MRL, µg/kg	4	4	30
LOD, µg/kg, QuEChERS-based method	1	0.5	2
LOQ, µg/kg, QuEChERS-based method	1	1	2
LOD, µg/kg, analyte fractionation method	0.5	0.5	4
LOQ, µg/kg, analyte fractionation method	0.5	1	4
	Penicillin G	Oxacillin	Cefalexin
MRL, µg/kg	4	30	100
LOD, µg/kg, QuEChERS-based method	0.5	2	10
LOQ, µg/kg, QuEChERS-based method	0.5	2	10
LOD, µg/kg, analyte fractionation method	0.5	2	10
LOQ, µg/kg, analyte fractionation method	1	4	20
	Cefapirin	Cefazolin	Ceftiofur
MRL, µg/kg	60	50	100
LOD, µg/kg, QuEChERS-based method	1	1	10
LOQ, µg/kg, QuEChERS-based method	1	1	10
LOD, µg/kg, analyte fractionation method	1	1	10
LOQ, µg/kg, analyte fractionation method	2	2	20
	Cefquinom	Cefalonium	Cefoperazone
MRL, µg/kg	20	20	50
LOD, µg/kg, QuEChERS-based method	10	10	5
LOQ, µg/kg, QuEChERS-based method	20	10	5
LOD, µg/kg, analyte fractionation method	10	10	5
LOQ, µg/kg, analyte fractionation method	20	20	5
	Erythromycin	Tylosin	Lincomycin
MRL, µg/kg	40	50	150
LOD, µg/kg, QuEChERS-based method	20	10	50
LOQ, µg/kg, QuEChERS-based method	20	20	50
LOD, µg/kg, analyte fractionation method	20	10	50
LOQ, µg/kg, analyte fractionation method	40	20	100
	Sulfamethazine	Sulfadoxine	Sulfamethoxypyridazine
MRL, µg/kg	100	100	100
LOD, µg/kg, QuEChERS-based method	15	15	15
LOQ, µg/kg, QuEChERS-based method	15	15	15
LOD, µg/kg, analyte fractionation method	15	15	15
LOQ, µg/kg, analyte fractionation method	30	30	30
	Tetracycline	Chlortetracycline	Oxytetracycline
MRL, µg/kg	100	100	100
LOD, µg/kg, QuEChERS-based method	25	25	25
LOQ, µg/kg, QuEChERS-based method	25	25	25
LOD, µg/kg, analyte fractionation method	25	25	25
LOQ, µg/kg, analyte fractionation method	50	25	50
	Marbofloxacin	Enrofloxacin	Ciprofloxacin
MRL, µg/kg	75	100	100
LOD, µg/kg, QuEChERS-based method	20	20	20
LOQ, µg/kg, QuEChERS-based method	20	20	20
LOD, µg/kg, analyte fractionation method	20	20	20
LOQ, µg/kg, analyte fractionation method	40	40	20
	Chlorate	Perchlorate	
MRL, µg/kg	100	100[a]	
LOD, µg/kg, QuEChERS-based method	10	2	
LOQ, µg/kg, QuEChERS-based method	10	2	
LOD, µg/kg, analyte fractionation method	5	0.5	
LOQ, µg/kg, analyte fractionation method	10	1	

[a] No official MRL available.

It can therefore be said that our fractionation method has a notable contribution to sustainability and represents a pathway to green chemistry in analytical laboratories.

As presented in the results and in Table 5 as a summarizing overview, FraMiTrACR also has other advantages, such as shorter working time for laboratory personnel to process the laboratory samples. With a run of 16 samples, the working time is reduced by 71% compared to QuPPe and by 87% compared to QuEChERS. Since working time contributes to the total cost per laboratory sample, such a large reduction represents a clear economic advantage for our fractionation method in analytical laboratories. This is also evident from the labor costs, which are reduced by similar levels of 70% compared to QuPPe and 84% compared to QuEChERS. Further cost savings are also conceivable (Table 4). For example, especially in laboratories routinely preparing high numbers of samples, eliminating the use of extraction agents, sorbents, and excess consumables will reduce the demand for storage space. This also reduces the complexity of inventory management. It can also be stated that laboratories using our fractionation method could process more laboratory samples at lower cost and with greater sustainability.

In Table 6, we have summarized analytical results from our previous studies that demonstrate the suitability of FraMiTrACR for the analytes shown. However, it should be considered that

our fractionation method is a newly developed one, which has not yet been tested for other analytes. Currently, the QuEChERS method offers a more diverse analytical spectrum, covering many analytes with different properties. The determination of such a wide range of analyses has not yet been shown for our fractionation method, although we have demonstrated that several different non-polar antibiotics and strongly polar pesticides could be determined in milk prepared with FraMiTrACR. In addition, the fractionation method has the advantage that no additives are introduced to the laboratory sample, so the risk of contamination is greatly reduced. The fractionation method also has the advantage that laboratory samples with different phases can be separated. In the future, we expect it is possible that our fractionation method will become established alongside the existing QuEChERS and QuPPe methods.

Conclusions

Our fractionation method using FraMiTrACR is an innovative one-step procedure for the preparation of laboratory samples with difficult matrixes. We have shown in previous publications that a wide range of analytes can be tested using this method. In the present study, we have also been able to demonstrate that using FraMiTrACR as an alternative to established methods enables more sustainable laboratory sample preparation and has economic advantages. In summary, compared to other methods, we achieved a reduction in the total weight of consumables and packaging required by up to 45% and a reduction in kg CO_2eq of up to 43%. In addition, our fractionation method offers up to 87% time-saving for laboratory personnel and up to an 84% reduction in labor costs per laboratory sample. We believe that FraMiTrACR is a pathway for green chemistry in the laboratory.

CRediT Author Statement

Jan-Michael Steils conceptualized the study, performed investigation and data analysis. Wrote, reviewed and edited the manuscript.
Alexander Kaluza conceptualized the study, performed investigation and data analysis. Wrote, reviewed and edited the manuscript.
Klaus Schöne conceptualized the study, performed investigation and data analysis. Wrote, reviewed and edited the manuscript.
John Cashman, native English speaker, reviewed and edited the manuscript.
Christian Baumgartner reviewed and edited the manuscript.
Maren Lang performed investigation and data analysis.
Melina Kraus performed investigation and data analysis.

Conflicts of Interest

The authors declare the following interests that may be considered as potential competing interests: Jan-Michael Steils and Christian Baumgartner are employed by pureMilk analytical, Alexander Kaluza, Klaus Schoene, and John Cashman are employed by Sartorius, and Maren Lang and Melina Kraus are employed by Milchprüfring Baden-Wurttemberg. However, these affiliations do not alter the authors' adherence to the scientific policies on sharing study results, data, and materials.

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