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Review

Exploring the Lipidome: Current Lipid Extraction Techniques for Mass Spectrometry Analysis

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Received: 7 April 2020; Accepted: 13 May 2020; Published: 3 June 2020

Abstract: In recent years, high-throughput lipid profiling has contributed to understand the biological, physiological and pathological roles of lipids in living organisms. Across all kingdoms of life, important cell and systemic processes are mediated by lipids including compartmentalization, signaling and energy homeostasis. Despite important advances in liquid chromatography and mass spectrometry, sample extraction procedures remain a bottleneck in lipidomic studies, since the wide structural diversity of lipids imposes a constrain in the type and amount of lipids extracted. Differences in extraction yield across lipid classes can induce a bias on down-stream analysis and outcomes. This review aims to summarize current lipid extraction techniques used for untargeted and targeted studies based on mass spectrometry. Considerations, applications, and limitations of these techniques are discussed when used to extract lipids in complex biological matrices, such as tissues, biofluids, foods, and microorganisms.

Keywords: extraction; lipids; untargeted lipidomics; targeted lipidomics

1. Introduction

The term lipids generally refers to amphiphilic organic molecules, poorly soluble in water but miscible in organic solvents. Classification and study of lipid species is challenging due to the large chemical and structural diversity, including different hydrocarbon backbone lengths, branching, unsaturations, and functional groups. Since 2005, the International Lipid Classification and Nomenclature Committee (ILCNC) on the initiative of the Lipid Metabolites and Pathways Strategy (LIPID MAPS) consortium defined lipids as "hydrophobic or amphipathic small molecules that originate entirely or in part by carbanion-based condensations of thioesters and/or by carbocation-based condensations of isoprene units" [1–3]. Current lipid classification involves eight categories based on chemical functionalities as: (1) glycerolipids (GL), (2) sphingolipids (SP), (3) glycerophospholipids (GP), (4) sterol lipids (ST), (5) fatty acyls (FA), (6) prenol lipids (PR), (7) polyketides (PK), and (8) saccharolipids (SL), where the last two categories are not synthesized by mammals and represent a small proportion of the known lipidome [1–3]. Table 1 presents the number of lipid structures per category according to Lipid Maps® Structure Database (LMSD) and Figure 1 shows representative structures for each category.

Table 1. Number of lipids structures per representative lipid category.

Lipid Category	Main Subclasses	Log P Range [a]	LIPID Maps [b]		
			Curated	Computationally-Generated	All
Fatty Acyls [FA]	Fatty Acids and Conjugates, Eicosanoids, Docosanoids, Fatty esters, Fatty amides, Fatty nitriles, Fatty ethers, Fatty acyl glycosides, Acylcarnitines.	−5–15	7644	1792	9436
Glycerolipids [GL]	Monoradylglycerols, Diradylglycerols, Triradylglycerols, Glycosylmonoradylglycerols, Glycosyldiradylglycerols.	5–35	232	7379	7611
Glycerophospholipids [GP]	Glycerophosphocholines, Glycerophosphoethanolamines, Glycerophosphoserines, Glycerophosphoglycerols, Glycerophosphoglycerophosphates, Glycerophosphoinositols, Oxidized glycerophospholipids, Cardiolipins.	5–25	1607	8312	9919
Sphingolipids [SP]	Sphingoid bases, Ceramides, Phosphosphingolipids, Neutral glycosphingolipids, Acidic glycosphingolipids, Basic glycosphingolipids.	5–25	1410	3176	4586
Sterol lipids [ST]	Sterols, Steroids, Secosteroids, Bile acids and derivatives, Steroid conjugates.	0–20	2829		2829
Prenol lipids [PR]	Isoprenoids, Quinones and hydroquinones, Polyprenols.	0–20	1352		1352
Saccharolipids [SL]	Acylaminosugars, Acylaminosugar glycans, Acyltrehaloses.	0–30	22	1294	1316
Polyketides [PK]	Linear polyketides, Macrolides and lactone polyketides, Linear tetracyclines, Polyether antibiotics, Aflatoxins, Flavonoids, Aromatic polyketides.	0–15	6810		6810
TOTAL			21,906	21,953	43,859

[a] Octanol/water partition coefficient (log P) calculated using ChemAxon. [b] Data taken from Lipid Maps® Structure Database (LMSD) in the 05/02/2020 update.

Once viewed as mere membranes constituents and energy storage reservoirs, nowadays lipids are also recognized for playing crucial roles in diverse biological activities at cellular and systemic levels including: cell signaling, transport, protein trafficking, growth, differentiation, and apoptosis [3,4]. To accomplish these myriad of functions, cells produce lipids with a vast structural complexity, along with a differentiated compartmentalization, location, organization and interaction [5]. Consequently, a particular set of lipids—known as lipidome—characterize each cell, tissue, and biological system [4].

Lipidomes are often are complex mixtures of lipids, with diverse chemical structures that represent the different biological microenvironments where lipids normally play their function in vivo. Therefore, lipidomes are highly susceptible to changes in response to physiological, pathological, and environmental conditions and can indicate an organism status in a particular moment [6]. In fact, abnormalities in the metabolism of lipids have been linked to several human pathologies (e.g., Alzheimer's disease [7], cancer [8], diabetes [9]), stress response in plants [10] and antibiotic resistance in infectious bacteria [11,12]. For this reason, the study of lipids has represented a valuable tool to elucidate mechanistic insights into all kingdoms of life.

The main analytical platforms for lipid analyses include mass spectrometry (MS) and nuclear magnetic resonance (NMR), where MS-based techniques have been widely used due to their high sensitivity (pM concentrations), availability and speediness in accurate identification, quantification and monitoring of basal lipid profiles in complex biological mixtures [13]. Sample preparation for MS-lipidomics usually includes solvent–protein precipitation, lipid extraction, and solvent evaporation. The initial step of protein precipitation aims to eliminate matrix components that could interfere with the precision and accuracy of the mass analysis, such as proteins and salts. The subsequent step of lipid extraction takes advantage of the hydrophobic properties of lipids to separate them in a non-polar solvent system with or without mechanical assistance (e.g., vortex, microwave, ultrasound). Finally, solvent evaporation allows lipid enrichment and resuspension in a compatible solvent for MS equipment, typically hyphenated to chromatographic separation [14].

Considering the analytical challenge of extracting hundreds of lipidic compounds with a wide range of polarities and concentration levels, there is not a unique method suitable to extract an entire lipidome. Thus, the choice of a particular lipid-extraction protocol must account for its inherent limitations and be tailored to a specific biological matrix, analysis approach and experimental design. The importance of this choice lies in the profound impact on the class of lipids that can be detectable and measured, which could create a bias on the subsequent analysis and findings. In general, two main approaches are used to analyze lipidomes: (1) non-targeted analysis, also known as hypothesis-generating, to simultaneously extract all detectable lipids in a sample regardless of class, concentration or prior identification, for which non-selective methods are used; (2) targeted analysis, or hypothesis-driven, to selectively extract a particular set of known lipids, in order to avoid interferences and enhance extraction efficiency [15].

Furthermore, repeatability and reproducibility during extraction should account for the lack of analyte-specific internal standards to asses lipid concentrations. In lipidomics, and metabolomics in general, multiple samples are analyzed under equivalent conditions to allow further comparison of analyte levels between different groups (e.g., control vs. disease) using univariate and multivariate statistical analysis. For this reason, biological variations most prevail over analytical and random variations in order to avoid data misinterpretation. In light of the vast diversity of lipids structures and its determining role in lipid extraction, this review summarizes current extraction protocols used for isolation of lipid species present in complex biological matrices, including microorganisms, biofluids, plant and animal tissues, and foods. Technical details concerning both, untargeted and targeted approaches, are discussed along with limitations and considerations of lipid extraction protocols employed in MS-based lipidomics.

2. Non-Targeted Analysis

Lipid extraction is without a doubt the major limiting step to analyze the complete set of lipids in biological systems under an untargeted approach. Liquid–liquid extraction (LLE) protocols based on chloroform/methanol mixtures, such as Folch [16] or Bligh and Dyer (BD) [17], have been widely used since the late 1950s with few modifications and still represent the benchmark in the field. Alternative LLE protocols include Methyl tert-butyl ether (MTBE) [18] and Butanol-methanol (BUME) [19] with comparable outcomes for lipid isolation in plasma samples [20,21]. The success of these protocols relies on exploiting the characteristic amphipathic properties of lipids to achieve a differential partition between an aqueous phase and an immiscible organic phase at given temperature, pH and ionic strength. In LLE protocols, separation in two phases is achieved by the hydrophobic and hydrophilic interactions within a system. Hydrophobic interactions are mediated by aliphatic and cyclic hydrocarbon backbones, while hydrophilic ones by polar groups, such as phosphates or carbohydrates. Lipids can also be isolated into one-phase systems, using either a single or a combination of miscible organic solvents for protein precipitation (PPT) and lipid solubilization. Methanol [22], isopropanol [23], and acetonitrile [24] have been proposed as organic systems for untargeted lipidomics.

Solid phase extraction (SPE) is also a feasible option for lipid extraction. It is based on a partition equilibrium involving the adsorption of lipids to a solid phase, which preconcentrates the hydrophobic compounds prior to desorption. Removal of interfering compounds and impurities is achieved by using SPE cartridges, commonly reverse-phase ones. The process comprises of cartridge conditioning, followed by sample loading, cartridge washing and elution. During these stages, aliphatic backbones in lipid structures interact with non-polar stationary phases (e.g., C8, C18) and are retained until an elution solvent is added. Although, SPE protocols are occasionally used for untargeted approaches, they are more typically used for targeted lipidomics. Other strategies for non-targeted lipid extraction are tailored to specific matrices (e.g., plants, cell lines), sampling (e.g., microextraction), and include the use of mechanical assistance like microwaves (MAE), ultrasound (UAE) among others [25]. Reports using solid phase microextraction (SPME) for comprehensive lipid analysis are also worth mentioning [26,27]. SPME employs sorbent-coated rods/fibers where lipids migrate and diffuse directly from a headspace or liquid, to the fiber or rod, eliminating the washing step required on SPE. Then, thermal or solvent desorption is used for lipid elution and analysis by gas chromatography-mass spectrometry (GC-MS) or liquid chromatography-mass spectrometry (LC-MS) respectively [28].

As shown in Figure 1, chemical structures across lipid classes display a large variety of polarities. Encompassing more than 10 units of log P in the octanol–water coefficient as a polarity index, the wide polarity window of lipid species is much wider than any solvent or solvent mixture can cover [15]. In consequence, none of the current protocols is capable to extract all lipid classes simultaneously with high recovery (>80%), and usually the yields of specific compounds are typically sacrificed at the expense of a wider coverage [13]. For instance, chloroform/methanol protocols can extract all lipid classes with recoveries higher than 50%, but present low recoveries for charged and non-polar lipids, like phosphatidic acids (PA) and lysophospholipids (LPA) in plasma [23,29].

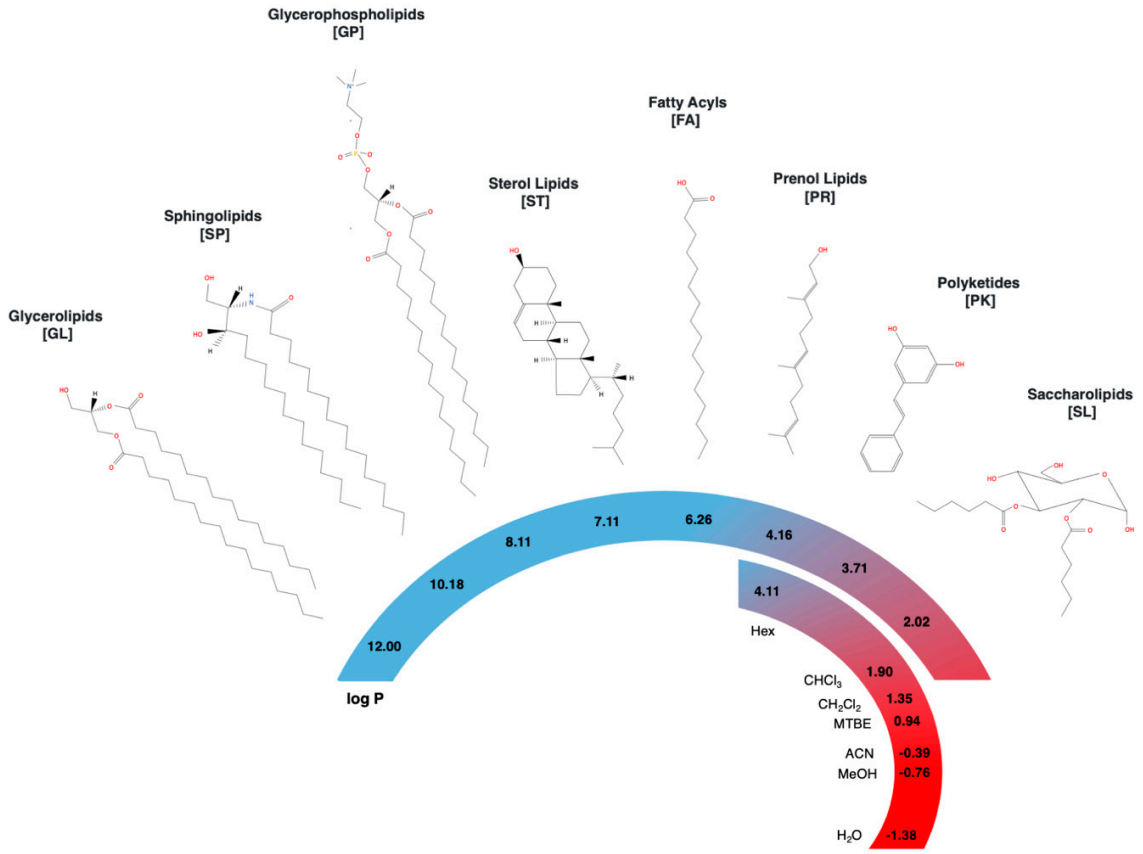

Figure 1. LIPID MAPS categories and representative structures with calculated octanol/water partition coefficient (log P) using ChemAxon. Reported log P of solvents used in lipidomics are indicated below [30]. Color code represents relative polarity, non-polar (blue), and polar (red). Example of classes corresponds to Glycerolipids, DG(16:0/16:0/0:0)—L02010001; Sphingolipids, SP(16:0/16:0)—LMGP01010564; Glicerophospholipids, PC(16:0/16:0)—LMGP01010564; Sterol lipids, Cholesterol—LMST01010001; Fatty acyls, C16:0—LMFA01010001; Prenol lipids, 2E,6E-farnesol—LMPR0103010001; Polyketides, Pinosylvin—LMPK13090001; Saccharolipids, 2,3-di-0-hexanoyl-α-glucopyranose—LMSL05000001.

Furthermore, the differential recovery across lipid species can interfere with the analysis to different extents. For example, a sub estimation of ST in cerebrospinal fluid is feasible due to its low concentration compared to major constituents FA and SP [31]. In contrast, a similar analysis in plasma would not have a significant impact on ST, considering the its relatively high concentration in that matrix. However, estimation of low-abundant FA could be affected, particularly oxylipins in the pM range [32]. For this reason, it is recommended to explore different extraction protocols if previous reports on the matrix of interest are not available. Crucial factors to be optimized include solvent system and sample-solvent ratio. A good example for method selection and validation can be found in the work of Van Meulebroek et al. [33].

One might tackle the low recovery limitation proposing sequential extraction steps, by using either the same or a complimentary solvent mixture. However, more extraction steps can introduce a higher systematic variability and increase the time of the procedure, which play a crucial factor in large-scale study settings. Furthermore, extraction protocols tend to be minimal in order to preserve sample integrity and content. Non-selective liquid extraction protocols, such as LLE are preferred to extract lipids, since these avoid harsh conditions that can lead to degradation products or cross-products. Nonetheless, there are some concerns about reproducibility of LLE protocols, in particular when MTBE is used given its high volatility [34]. Therefore, single-phase [23,34,35] and even triphasic systems [36] have been proposed to achieve enhanced reproducibility and lipid coverage. Further validation of

these methodologies is still required. Table 2 presents a contrast of current lipid extraction protocols used for untargeted MS-based studies of biological matrices. Different parameters were taking into account for the comparison, including coverage, recovery, reproducibility and automatization. Note that lipidomic studies using matrix-assisted laser desorption-ionization (MALDI) as ionization source were not included in this review (recently reviewed by Leopold et al. [37]), since little or no sample preparation is needed.

Table 2. Comparison between extraction methods used in mass spectrometry (MS)-based untargeted lipidomics.

Extraction Method	Principle	Protocol Name	System	Lipid Coverage	Lipid Recovery	Solvent-Efficiency	Carry-Over Free	Time-Efficiency	Repeatability	Versatility	Automatization	Biological Matrix	Platform	Ref.
PPT	Precipitation	OPE	*i*PrOH, ButOH/MeOH (2:2) $CHCl_3$/MeOH (2:2)									Plasma	HPLC-ESI-QTRAP	[38–40]
												CSF	UHPLC-ESI-QTOF	[41]
LLE	Partition	Folch *	$CHCl_3$/MeOH (2:1)									Cell line/tissue	UHPLC-ESI-Q-Exactive Orbitrap	[42]
												CSF	HPLC-ESI-Q-Exactive Orbitrap	[43]
		Folch * BD *	$CHCl_3$/MeOH (2:1) $CHCl_3$ or CH_2Cl_2/MeOH (1:2)									Plasma/CSF Food	HPLC-ESI-Ion trap	[44]
													UHPLC-Q-Exactive Orbitrap	[45, 46]
												Tears	UHPLC-TripleTOF	[47]
												Plants	HPLC-ESI-QTOF	[48]
												Urine	UHPLC-ESI-3D-Ion trap	[49]
												Feces	HPLC-ESI-Q-Exactive Orbitrap	[50]
												Cell culture	HPLC-ESI-Q-Exactive Orbitrap	[43]
		BD * MTBE *	$CHCl_3$ or CH_2Cl_2/MeOH (1:2) MTBE/MeOH (5:1.5)									Animal tissue	DI-ESI-QTRAP	[51]
												Urine/saliva	ASAP-QTOF	[52]
												Plant tissue	UHPLC-ESI-IT-TOF	[53, 54]
												Feces	HPLC-ESI-Q-Exactive Orbitrap	[50]

Table 2. *Cont.*

Extraction Method	Principle	Protocol Name	System	Lipid Coverage	Lipid Recovery	Solvent-Efficiency	Carry-Over Free	Time-Efficiency	Repeatability	Versatility	Automatization	Biological Matrix	Platform	Ref.
		MTBE * BUME	MTBE/MeOH (5:1.5) 1. ButOH/MeOH (3:1) 2. Hep/EtOAc (3:1) 3. 1% AcOH									Plasma	HPLC-ESI-QTOF	[55]
												Urine	HPLC-ESI-QTOF	[56]
												Food	UHPLC-ESI-TOF	[57]
												Breast Milk	HPLC-ESI-QTOF	[58]
												Plant tissue	UHPLC-ESI-Q-Exactive Orbitrap	[59]
												Cell line	HPLC-LTQ-Orbitrap	[60]
												Plant tissue	UHPLC-ESI-Q-Exactive Orbitrap	[61]
													UHPLC-ESI-QTOF	[62]
												Cell line Plasma/SBF	HPLC-ESI-QqQ	[63]
												Animal tissue	DI-ESI-QTRAP	[51]
		BUME IPA/Hex *	1. ButOH/MeOH (3:1) 2. Hep/EtOAc (3:1) 3. 1% AcOH*i*PrOH/Hex (3:2)									Cell lines	UHPLC-ESI-Q-Exactive Orbitrap	[64]
												Cell lines	UHPLC-ESI-Q-Exactive Orbitrap	[61]
												Cell lines	UHPLC-ESI-QTOF	[62]
		IPA/Hex * SFE	*i*PrOH/Hex (3:2) Supercritical CO_2									Serum	DI-ESI-TOF	[65]
												Parasites	HPLC-ESI-QqQ	[66]
												Plasma	SFE-ESI-QTRAP	[67]
												Parasites	UHPSFC-ESI-IT-TOF	[68]

Table 2. *Cont.*

Extraction Method	Principle	Protocol Name	System	Lipid Coverage	Lipid Recovery	Solvent-Efficiency	Carry-Over Free	Time-Efficiency	Repeatability	Versatility	Automatization	Biological Matrix	Platform	Ref.
		SPE	Coated fibers and capillary tubes (sorbent cartridge).									Animal tissue Plasma	UHPSFC-ESI-IT-TOF	[69]
													HPLC-ESI-Q-Exactive Orbitrap	[70]
SPE	Adsorbance	SPE SPME	Coated fibers and capillary tubes (sorbent cartridge). Diameter-reduced sorbent-coated rods/fibers									Saliva	HPLC-ESI-Q-Exactive Orbitrap	[71]
												Breast Milk	HPLC-ESI-QTOF	[72]
												Cell lines	HPLC-ESI-Q-Exactive Orbitrap	[43]
												Urine	GC-EI-Q	[26, 27]

* Water is added for phase separation. OPE: One-phase extraction; PPT: Protein precipitation; BD: Bligh and Dyer; SFE: Supercritical fluid extraction; SPE: Solid-phase extraction; SPME: Solid-phase microextraction; BUME: Butanol-methanol; MTBE: Methyl tert-butyl ether; DI: Direct infusion; ASAP: Atmospheric Solids Analysis Probe; Color reference: Dark blue: Good; Blue: Fair; Light blue: Poor. References were selected for studies conducted during the 2009–2019 period.

In recent years, automatized lipid extraction has been proposed to decrease the experimental variability between samples in large batches. Not all solvent–extraction systems are suitable for this task, since some of them are prone to contamination with proteins and other matrix components. This is the case of chloroform/methanol protocols, where in order to get access to the non-polar fraction at the bottom, the injection needle must break through a protein interphase and a polar fraction at the top. In contrast, MTBE and BUME methods use a low-density extraction solvent that locates the hydrophobic fraction at the top of the partition system, there it can be easily sampled by an automatized needle. Moreover, solvent compatibility with the MS system should be considered. For instance, chloroform is well-known for being problematic with liquid chromatography (LC)-MS and it has to be removed by a previous injection. One-phase extraction (OPE) and SPE protocols could also be automatized for high throughput analysis. A recent review by Liu et al. covers the details and advances in analytical methods for MS-based large-scale lipidomics [73].

Another consideration is the high sensitivity of MS instruments, which could play a double-edged sword role in the mass-to-charge analysis of lipid extracts. On the one hand, small sample amounts are enough to detect femtomolar and quantify picomolar concentrations of lipid species. Usually only 10–100 μL of liquid sample or 1–100 mg of solid sample is required for lipid extraction. Then, 5–20 μL of extract are subsequently taken for either LC injection (LC-MS based lipidomics) or direct infusion into an MS (also called shotgun lipidomics). On the other hand, multi-sourced trace impurities coming from biological matrices (e.g., remaining proteins), solvents, preparation devices (e.g., siloxenes and phthalates), and even sample containers (e.g., plasticizers) can also be detected if carried over in the lipid extract.

Overall, the presence of contaminants excerpts an effect on ionization (either enhancement or suppression) and can lead to deterioration of MS instrumentation. This issue is not as critical in LC-MS methods as in shotgun lipidomics, since LC allows separation between lipids and contaminants. Consequently, HPLC (high-performance liquid chromatography) and UPLC (ultra-performance liquid chromatography) are commonly preferred for non-directed lipidomics at the expense of increased solvent consumption and analysis time. Recently, SFC (supercritical fluid chromatography) have been successfully applied as a sample separation step to overcome these drawbacks [74].

Although, a comprehensive discussion of sampling and sample processing falls outside the scope of this review, general guidelines for handling biological matrices are implemented to preserve lipidome integrity. These measures include sample storage at −80 °C, avoid freeze–thaw cycling, and short processing times at 4 °C to minimize unwanted enzymatic and chemical processes. However, some lipid species (e.g., oxylipins, polyphenols, lysoGP) require particular measures due to their susceptibility to oxidation and isomerization. For this reason, antioxidants such as, butylated hydroxytoluene (BHT), butylated hydroxyanisole (BHA), or triphenylphosphonium (TPP), along with buffers are commonly included prior sample homogenization and extraction. Additionally, the use of MS grade solvents, glass vials and glass pipetting tips significantly decrease the incorporation of contaminants.

Another important limitation of any current extraction protocol is the inherent homogenization of lipids coming from different sub-compartments (e.g., tissue region, cell type, organelles). The disruption of in vivo interactions and subsequent reorganization of lipids by hydrophobicity not only hinders the chance to localize and monitor its dynamic changes, but also can impact its stability and reactivity [13]. Therefore, conclusions from these studies most acknowledge this limitation in the biological interpretation of their outcomes.

Overall, lipidomic studies can be powerful hypothesis-generating tools. Extraction conditions should be adjusted and validated for the biological matrix of interest. General guidelines include testing of repeatability, reproducibility, and recovery using at least one representative compound per lipid class. The step by step workflow for protocol selection proposed by Furse et al. [75] can serve as a starting point.

3. Targeted Analysis

For studies focused on a specific subset of lipids, the particular features in their chemical structures drive the selection of the extraction protocol. Isolation and concentration of lipids of interest is achieved by either LLE with narrow polarity windows or SPE cartridges. Compared with untargeted approaches, targeted analysis allows higher sample amounts due to the selective procedures used for enrichment of a particular lipid species. For instance, to study low-abundant oxylipins in plasma, up to 250 μL of the sample are extracted, which represents ten times the typical amount used for untargeted approaches [14].

In general, compounds with a high hydrophobicity index, such as triacylglycerols (TG), diacylglycerols (DG), cholesteryl esters and fatty esters, are commonly extracted with LLE. Non-polar solvents (e.g., cyclohexane, toluene) are preferred over moderately polar solvent mixtures (e.g., chloroform, MTBE) since only the most hydrophobic lipids dissolve in them [75].

The extraction of intermediate hydrophilic species, such as GP and SP, is usually achieved by LLE using polar solvents. Chloroform-based protocols are the most common, followed by a rising popularity of MBTE-based ones. Considering the recovery disparities across lipid species, these protocols are often modified to achieve higher extraction yields, including changes in solvent system, solvent proportions (%v/v), and introduction of mechanic forces. When charged groups are present, another important variable is the pH, since the acid-base character of certain lipids can be used for its extraction and enrichment. For instance, phosphatidic acids (PA), phosphatidylserines (PS) [76] and phosphatidylinositols (PI) [77] can be efficiently extracted using mild acidic conditions. However, pH changes must be optimized to avoid structural re-arrangements in the presence of nucleophiles, given the high electrophilicity of phosphate groups [78].

Finally, isolation of polar lipids has less standardized protocols given both, the similarities in physicochemical properties to common non-lipid metabolites and the complex structure of these compounds (e.g., acylaminosugars, cerebrosides). Typical approaches use water, methanol, or pyrimide as polar solvents in combination with additives [75]. When SPME is used, derivatization reagents are incorporated into the SPME fibers to improve specificity and sensitivity. Table 3 provides a revision of recent lipidomic targeted studies in different biological matrices. A discussion for each lipid category is also presented.

Table 3. Reports of targeted extraction of lipids by category.

Lipid Class	Extraction Method	System	Biological Matrix (Sample Amount)	Platform	Ref
Fatty Acyls					
Fatty Acids and Conjugates					
	1. LLE, 2. SPE	1. Modified Bligh and Dyer, CH_3Cl - MeOH - H_2O (1:1:1) with 2 mM HCl; 2. 3-aminopropyl silica gel/ACN-AcOH (49:1)	Food supplements (3 mL)	UHPLC-ESI-QTOF	[79]
	LLE	H_2O with 0.5 M HCl - anhydrous Et_2O (1:1) + Deriv. with BSTFA	Feces (30 mg)	GC-Q	[80]
	LLE	Modified Folch, CH_3Cl-MeOH-H_2O (2:1:0.8) + BHT	Grapes-skins-seeds (0.1 g)	UHPLC-ESI-QqQ	[81]
	LLE	Modified Folch, CH_3Cl - MeOH - 0.73% NaCl (2:1:0.6) + Deriv. with 1% H_2SO_4 in MeOH	Green coffee (0.5 g)	GC-Q	[82]
	LLE	Hex - 0.5% NaOH in MEOH and 14% BF_3 in MeOH - Sat. NaCl (1.3:2:4)	Shark liver oil (25 mg)	GC-Q	[83]
	1. Filter pre-conc. 2. LLE	1. Whatman GF/F filters, 2. CH_2Cl_2 - MeOH - H_2O (1.5:3:1)	Oceanic water (5–10 L)	DI-ESI- FT-ICR MS	[84]
Octadecanoids					
	1. OPE, 2. SPE	1. MeOH + BHT; 2. < 8% MeOH/Polymeric RP/MeOH + BHT	Mice amygdala tissue	UHPLC-ESI-QTRAP	[85]
Eicosanoids					
	1. LLE, 2. Hydrolysis, 3. SPE	1. MTBE-MeOH-0.15 M NH_4OAc (2:1:1) + BHT; 2. MeOH-H_2O-10M NaOH (1:1:1.2); 3. Reac.Mix. + AcOH + 0.1 M Na_2HPO_4 buffer (pH 6)/AEC/tOAc-Hex (75:25) + 1%AcOH	Human cells (1×10^7)	HPLC-ESI-QTRAP	[86]
	LLE	Sample + AcOH (pH 3.5) - MTBE (2:1) + Deriv. for GC	Breath condensate (2 mL)	HPLC-ESI-QTRAP GC/NICI–MS	[87]
	SPE	MeOH (<17%) + Na_2HPO_4 buffer (pH 6)/AEC/EtOAc - Hex (75:25) with 1% AcOH	Plasma (500 µL)	UHPLC-ESI-QTRAP	[86]
	SPE	H_2O + BHT/Polymeric RP/MeOH	Plasma (500 µL)	UPLC-ESI-QqQ	[88]
	SPE	15% MeOH + 0.1 M HCl (pH 3.0)/C18/Methyl formate	Mouse brain tissue (25–75 mg)	HPLC-ESI-QqQ	[89, 90]
	SPE	10% MeOH/Polymeric RP/MeOH	Human cells-animal tissues	HPLC-ESI-QTRAP	[91]

Table 3. *Cont.*

Lipid Class	Extraction Method	System	Biological Matrix (Sample Amount)	Platform	Ref
	1. OPE, 2. SPE	1. MeOH + BHT; 2. < 8% MeOH/Polymeric RP/MeOH + BHT	Mice brain tissue	UHPLC-ESI-QTRAP	[85]
	SPE	0.12 M PP buffer + 5 mM $MgCl_2$ + BHT/Polymeric RP/MeOH	Human CSF and rat cortex	UPLC-ESI-QqQ	[92]
Fatty Esters					
	OPE	MeOH - 0.1% FA (0.8:1)	Plasma (20 µL)-urine (5 µL)-CSF (20 µL)	UHPLC-HESI-QTRAP	[93]
	1. OPE, 2. OPE	1. MeOH - H_2O (4:1) + 0.1% FA; 2. MeOH - 0.1% FA (0.8:1)	Human brain tissue (10 mg)	UHPLC-HESI-Q-Orbitrap	[93]
	OPE	*i*PrOH	Serum (10 µL)	HPLC-ESI-QqQ	[94]
	OPE	AbsoluteIDQ p180 Kit	Serum (10 µL)	HPLC-ESI-QqQ	[95]
	OPE	AbsoluteIDQ p180 Kit	Plasma	UPLC-ESI-QqQ	[96]
	OPE	ACN + Deriv. with DnsHz	Plasma	UHPLC-ESI-QqQ	[97]
	1. LLE, 2. SPE	1. $CHCl_3$ - MeOH - PBS (2:1:1); 2./$CHCl_3$/Silica NP/EtOAc	Adipose tissue (150 mg)	HPLC-ESI-QqQ	[98]
	1. LLE, 2. SPE	1. $CHCl_3$ - MeOH - PBS (2:1:0.86); 2./$CHCl_3$/Silica NP/EtOAc	Serum or plasma (200 µL)	HPLC-ESI-QqQ	[98]
	1. LLE, 2. SPE	1. Bligh and Dyer, $CHCl_3$-MeOH - H_2O (2:1:1); 2. 0.1% NH_4OH in ACN/AEC/1% FA in Acetone + AMPP	Plant leaves (100 mg)	UHPLC-ESI-QqQ	[99]
	SPE	0.1% NH_4OH in ACN (1:2)/AEC/1% FA in Acetone + Deriv. DMED and d4-DMED	Mice adipose tissue (100 mg)	UHPLC-ESI-QqQ	[100]
	1. LLE, 2. SPE	1. Modified Bligh and Dyer, $CHCl_3$ - MeOH (1:1); 2. $CHCl_3$/Silica NP/EtOAc	Plasma (100 µL), liver	nanoESI-QqQ	[101]
Fatty amides					
	SPE	10% MeOH/Polymeric RP/MeOH	Human cell lines or animal tissues	HPLC-ESI-QTRAP	[91]
	SPE	MeOH - H_2O (1:2.3)/C18/MeOH	Rat brain	HPLC-ESI-QqQ	[102]

Table 3. *Cont.*

Lipid Class	Extraction Method	System	Biological Matrix (Sample Amount)	Platform	Ref
Glycerolipids					
Monoradylglycerols					
	OPE	MeOH + Deriv. with d_4-NPB and 3-NPB	Cells-Tissue (60 mg)-Serum (50 µL)	UPLC-ESI-QTOF	[103]
	OPE	*i*PrOH	Shark liver oil (10 mg)	HPLC-ESI-QqQ	[83]
	1. Filter pre-conc. 2. LLE	1. Whatman GF/F filters, 2. CH_2Cl_2 - MeOH - H_2O (1.5:3:1)	Oceanic water (5–10 L)	DI-ESI- FT-ICR MS	[84]
	LLE	$CHCl_3$ - MeOH - 25 M LiCl (1:1:1)	Plasma (25 µL)	DI-ESI-QTOF	[104]
Diradylglycerols					
	1. OPE, 2. LLE	1. 70% *i*PrOH, 2. Bligh and Dyer	Feces (2 mg)	FIA-ESI-Q-Orbitrap	[105]
	OPE	*i*PrOH	Shark liver oil (10 mg)	HPLC-ESI-QqQ	[83]
	LLE	Modified Bligh and Dyer, $CHCl_3$ - MeOH - H_2O (1:1:0.8)	Bacterial cells (OD: 0.3, 0.5, 0.8, 1.3)	HPLC-ESI-LTQ-Orbitrap	[106]
	LLE	Modified Matyash, MTBE - MeOH - H_2O (3:0.9:0.75)	Skeletal muscle (50 mg)	HPLC-API-QqQ	[107]
	1. Filter pre-conc. 2. LLE	1. Whatman GF/F filters, 2. CH_2Cl_2 - MeOH - H_2O (1.5:3:1)	Oceanic water (5–10 L)	DI-ESI- FT-ICR MS	[84]
Triradylglycerols					
	LLE	Modified Bligh and Dyer, CH_2Cl_2 - MeOH - H_2O (1.5:3:1)	Serum (30 µL)	HPLC-HESI-Orbitrap	[108]
	OPE	EtOH - MTBE - DCM (70:15:15)	Size-fractionated serum (20 µL)	UPLC-ESI-QTRAP	[35]
	LLE	Modified Bligh and Dyer, $CHCl_3$ - MeOH - H_2O (1:1:0.8)	Bacterial cells (OD: 0.3, 0.5, 0.8, 1.3)	HPLC-ESI-LTQ-Orbitrap	[106]
	OPE	Acetone	Vegetal Oil (40 mg)	HPLC-ESI-Quadrupole	[109]
	1. Filter pre-conc. 2. LLE	1. Whatman GF/F filters, 2. CH_2Cl_2 - MeOH - H_2O (1.5:3:1)	Oceanic water (5–10 L)	DI-ESI- FT-ICR MS	[84]
	1. OPE, 2. LLE	1. 70% *i*PrOH, 2. Bligh and Dyer	Feces (2 mg)	FIA-ESI-Q-Orbitrap	[105]

Table 3. *Cont.*

Lipid Class	Extraction Method	System	Biological Matrix (Sample Amount)	Platform	Ref
Glycosyldiradylglycerols					
	1. pre-treat, 2. LLE	1. *i*PrOH (75 °C) + BHT; 2. $CHCl_3$ - MeOH (2:1)	Vegetal tissue (2–3 plant rosettes)	ESI-QqQ	[110]
	LLE	Bligh and Dyer	Algae tissue (30 L culture)	UPLC-ESI-QTOF	[111]
Glycerophospholipids					
Glycerophosphocholines					
	OPE	AbsoluteIDQ p150 Kit	Plasma (10 µL)	FIA-ESI-QTRAP	[112]
	OPE	ACN	Plasma (20 µL)	UPLC-ESI-QTRAP	[113]
	OPE	MeOH + BHT	Plasma (10 µL)	HPLC-ESI-QTRAP	[114]
	LLE	CH_2Cl_2 - MeOH (2:1)	Cytosol (100 µL)	UPLC-ESI-QTRAP	[115]
	LLE	Modified Folch, $CHCl_3$ - MeOH - 0.15 M NaCl (2:1:0.8) + BHT	Lenses	ESI-QqQ	[116]
	LLE	Modified Bligh and Dyer, $CHCl_3$ - MeOH - 0.1N HCl (1:1:1)	Human cells (2×10^6)	UPLC-ESI-QTOF	[117, 118]
	µChip-SPE	Lysozyme in 20 mM Tris-HCl (pH 7.5)/Silica beads/MeOH	Bacterial cells (10µL)	nanoESI-QTOF	[119]
	OPE	EtOH - MTBE - DCM (7:1.5:1.5)	Size-fractionated serum (20 µL)	UPLC-ESI-QTRAP	[35]
	LLE	Bligh and Dyer	Algae tissue (30 L culture)	UPLC-ESI-QTOF	[111]
Glycerophosphoethanolamines					
	OPE	ACN	Plasma (20 µL)	UPLC-ESI-QTRAP	[113]
	OPE	MeOH + BHT	Plasma (20 µL)	HPLC-ESI-QTRAP	[114]
	LLE	CH_2Cl_2 - MeOH (2:1)	Cytosol (100 µL)	UPLC-ESI-QTRAP	[115]
	LLE	Modified Folch, $CHCl_3$ - MeOH - 0.15 M NaCl (2:1:0.8) + BHT	Lenses	DI-ESI-QqQ	[116]
	LLE	Modified Bligh and Dyer, $CHCl_3$ - MeOH - 0.1N HCl (1:1:1)	Human cells ($2 \text{ X } 10^6$)	UPLC-ESI-QTOF	[117, 118]
	µChip-SPE	Lysozyme in 20 mM Tris-HCl (pH 7.5)/Silica beads/MeOH	Bacterial cells (10 µL)	nanoESI-QTOF	[119]

Table 3. *Cont.*

Lipid Class	Extraction Method	System	Biological Matrix (Sample Amount)	Platform	Ref
	OPE	EtOH - MTBE - DCM (7:1.5:1.5)	Size-fractionated serum (20 µL)	UPLC-ESI-QTRAP	[35]
	LLE	Bligh and Dyer	Algae tissue (30 L culture)	UPLC-ESI-QTOF	[111]
Glycerophosphoserines					
	OPE	ACN	Plasma (20 µL)	UPLC-ESI-QTRAP	[113]
	LLE	CH_2Cl_2 - MeOH (2:1)	Cytosol (100 µL)	UPLC-ESI-QTRAP	[115]
	LLE	Bligh and Dyer	Human cells (0.4×10^6)	ESI-QTRAP	[120]
	LLE	Modified Folch, $CHCl_3$ - MeOH - 0.15 M NaCl (2:1:0.8) + BHT	Lenses	ESI-QqQ	[116]
	µChip-SPE	Lysozyme in 20 mM Tris-HCl (pH 7.5)/Silica beads/MeOH	Bacterial cells (10µL)	nanoESI-QTOF	[119]
Glycerophosphoglycerols					
	OPE	ACN	Plasma (20 µL)	UPLC-ESI-QTRAP	[113]
	LLE	Modified Bligh and Dyer, $CHCl_3$ - MeOH - 0.1N HCl (1:1:1)	Human cells (0.4×10^6)	UPLC-ESI-QTOF	[117, 118]
	µChip-SPE	Lysozyme in 20 mM Tris-HCl (pH 7.5)/Silica beads/MeOH	Bacterial cells (10 µL)	nanoESI-QTOF	[119]
	LLE	Modified Bligh and Dyer, $CHCl_3$ - MeOH - H_2O (1:1:0.8)	Bacterial cells (OD: 0.3, 0.5, 0.8, 1.3)	UPLC-ESI-QqQ	[106]
	LLE	Bligh and Dyer	Algae tissue (30 L culture)	UPLC-ESI-QTOF	[111]
Glycerophosphoinositols					
	OPE	ACN	Plasma (20 µL)	UPLC-ESI-QTRAP	[113]
	LLE	CH_2Cl_2 - MeOH (2:1)	Cytosol (100 µL)	UPLC-ESI-QTRAP	[115]
	LLE	Modified Bligh and Dyer, $CHCl_3$ - MeOH - 0.1N HCl (1:1:1)	Human cells (2×10^6)	UPLC-ESI-QTOF	[117, 118]
	µChip-SPE	Lysozyme in 20 mM Tris-HCl (pH 7.5)/Silica beads/MeOH	Bacteria Cells (10 µL)	nanoESI-QTOF	[119]
	OPE	EtOH - MTBE - DCM (7:1.5:1.5)	Size-fractionated serum (20 µL)	UPLC-ESI-QTRAP	[35]

Table 3. *Cont.*

Lipid Class	Extraction Method	System	Biological Matrix (Sample Amount)	Platform	Ref
Glycerophosphates					
	OPE	ACN	Plasma (20 µL)	UPLC-ESI-QTRAP	[113]
	µChip-SPE	Lysozyme in 20 mM Tris-HCl (pH 7.5)/Silica beads/MeOH	Bacterial cells (10µL)	nanoESI-QTOF	[119]
Glycerophosphoglycerophosphoglycerols					
	LLE	Modified Bligh and Dyer, $CHCl_3$ - MeOH - H_2O (1:1:0.8)	Bacterial cells (OD: 0.3, 0.5, 0.8, 1.3)	HPLC-ESI-QTOF	[106]
Oxidized glycerophospholipids					
	µHP-SPE	MeOH/C18 spin column/MeOH - 0.2% FA (82:18)	Plasma (20 µL)	HPLC-ESI-QTRAP	[121]
Sphingolipids					
Sphingoid bases					
	LLE	Modified Bligh and Dyer, $CHCl_3$ - MeOH -H_2O (1.8:2:0.8) + 0.1% TFA	Plasma (50 µL)	UHPLC-ESI-QqQ	[122]
	LLE	Bligh and Dyer, $CHCl_3$ - MeOH - H_2O (1:2:0.8)	B Cells (80 µL cell suspension)	HPLC-ESI-QTRAP	[123]
	LLE	MTBE - MeOH - H_2O (3:0.9:0.8)	Plasma-Red blood cells (50 µL)	UHPLC-ESI-QqQ	[124]
	LLE + Transesterification	0.25M MeONa in MeOH - MTBE - H_2O (1.3:4:1) + AcOH (pH 7)	Serum (40 µL)	UHPLC-ESI-QqQ	[125]
	LLE + Sap.	CH_2Cl_2 - MeOH - KOH 1M in MeOH (1:2:0.3)	Cells (10^6)-Tissue (1–10 mg)	LC-MS/MS techniques	[126]
	LLE	CH_2Cl_2 - MeOH (1:1) with 0.25% DEA	Plasma (25 µL)	HPLC-ESI-QqQ	[127]
	LLE	ButOH - 40 mM Na_2HPO_4 + CA (pH4) (1:1)	Plasma (75 µL)	HPLC-ESI-QTRAP	[128]
Ceramides					
	LLE	Modified Bligh and Dyer, $CHCl_3$ - MeOH -H_2O (1.8:2:0.8) + 0.1% TFA	Plasma (50 µL)	UHPLC-ESI-QqQ	[122]
	LLE	Bligh and Dyer, $CHCl_3$ - MeOH - H_2O (1:2:0.8)	B Cells (80 µL cell suspension)	HPLC-ESI-QTRAP	[123]

Table 3. *Cont.*

Lipid Class	Extraction Method	System	Biological Matrix (Sample Amount)	Platform	Ref
	LLE + Sap.	$CHCl_3$ - MeOH - 1M KOH in MeOH (1:2:0.3)	Cells (10^6)-Tissue (1–10 mg)	LC-MS/MS techniques	[126]
	LLE	CH_2Cl_2 - MeOH (1:1) with 0.25% DEA	Plasma (25 µL)	HPLC-ESI-QqQ	[127]
	LLE + Transesterification	0.25M MeONa in MeOH - MTBE - H_2O (1.3:4:1) + AcOH (pH 7)	Serum (40 µL)	UHPLC-ESI-QqQ	[125]
	LLE	ButOH - 40 mM Na_2HPO_4 + CA (pH4) (1:1)	Plasma (75 µl)	HPLC-ESI-QTRAP	[128]
	1. OPE, 2. SPE	1.MeOH, 2.Hex-*i*PrOH (11:1)/aminopropyl silica cartridges/Hex-$CHCl_3$-MeOH (80:10:10)	Skin (Three patches)	UHPLC-ESI-QTOF	[129]
Phosphosphingolipids					
	LLE	Modified Bligh and Dyer, $CHCl_3$ - MeOH -H_2O (1.8:2:0.8) + 0.1% TFA	Plasma (50 µL)	UHPLC-ESI-QqQ	[122]
	LLE	$CHCl_3$ - MeOH - 1M KOH in MeOH (1:2:0.3)	Cells (10^6)-Tissue (1–10 mg)	LC-MS/MS techniques	[126]
	LLE + Transesterification	0.25M MeONa in MeOH - MTBE - H_2O (1.3:4:1) + AcOH (pH 7)	Serum (40 µL)	UHPLC-ESI-QqQ	[125]
	OPE	MeOH	Whole blood (15 µL on DBS)	UHPLC-ESI-TOF	[130]
	OPE	AbsoluteIDQ p150 Kit	Plasma (10 µL)	FIA-ESI-QTRAP	[112]
Neutral glycosphingolipids					
	LLE	Bligh and Dyer, $CHCl_3$ - MeOH - H_2O (1:2:0.8)	B Cells (80 µL cell suspension)	HPLC-ESI-QTRAP	[123]
	LLE	$CHCl_3$ - MeOH - 1M KOH in MeOH (1:2:0.3)	Cells (10^6)-Tissue (1–10 mg)	LC-MS/MS techniques	[126]
	LLE	ButOH - 40 mM Na_2HPO_4 + CA (pH 4) (1:1)	Plasma (75 µL)	HPLC-ESI-QTRAP	[128]
	LLE	MTBE - MeOH - H_2O (3:0.9:0.8)	Plasma-Red blood cells (50 µL)	UHPLC-ESI-QqQ	[124]
Acidic glycosphingolipids					
	LLE	$CHCl_3$ - MeOH - H_2O (0.8:1:1) + Deriv. with PAEA and DMTMM to aq. phase	Plasma (20 µL)	UHPLC-ESI-QTRAP	[131]

Table 3. *Cont.*

Lipid Class	Extraction Method	System	Biological Matrix (Sample Amount)	Platform	Ref
	1. LLE, 2. SPE	1. Modified Folch, $CHCl_3$ - MeOH -H_2O (2:1:0.6) 2.C18/MeOH to aq. phase	Plasma (200 µL)-Human tissues (25 mg)	HPLC-ESI-QTOF	[132]
	LLE	CH_2Cl_2 - MeOH (1:1) with 0.25% DEA	Plasma (25 µL)	HPLC-ESI-QqQ	[127]
Sterol lipids					
Sterols					
	SPE	Hex - Et_2O (99:1)/NP silica cartridge/Hex - Et_2O (99:1)	Sunflower oils (200 mg)	ESI-QTRAP-QqQ	[133]
	SPE	*i*PrOH/Polymeric RP/MeOH - 0.02% FA (10:90)	Plasma-Serum-CSF (100 µL)	HPLC-ESI-QTRAP	[134]
	LLE	Bligh and Dyer like method + Deriv. with AcCl - $CHCl_3$ (1:5)	Ocular Tissue	HPLC-ESI-QTrap-Orbitrap	[135]
	1. OPE + Esterif. 2. LLE	1. *i*PrOH 70% + 5M NaOH (1M HCl), 2. *i*Oct - Reaction Mix. (2:1) + Deriv. with MSTFA	Feces (2 g)	GC-QqQ	[136]
	1. OPE + Esterif. 2. LLE	1. *i*PrOH 70%+5M NaOH (1M HCl), 2. *i*Oct-Reaction Mix.(2:1)+Deriv. with DMG+DMAP	Feces (2 g)	UHPL-HESI-Q-Orbitrap	[137]
	LLE	Hex - *i*PrOH - 0.47M Na_2SO_4 (2:3:1.5) + BHT	Atherosclerotic plaques (10 mg)	HPLC-APCI-QqQ	[138]
	1. OPE, 2. LLE	1. 50 mM Tris-HCl (pH 7.5), 150 mM NaCl and 2mM EGTA, 2. Modified Bligh and Dyer, $CHCl_3$ - MeOH - Sample (1:1:0.9)	Silkworm tissues	HPLC-ESI-QqQ	[139]
Steroids					
	LLE	MTBE	Serum (100 µl)	HPLC-ESI-QTRAP	[140]
	SLE	Acetate buffer (pH 5.2)/Diat. Earth/CH_2Cl_2 + Deriv. with MSTFA - NH_4I – DTE (500:4:2)	Serum (100 µl)	GC-QqQ	[141]
	SPE	5% H_3PO_4/Polymeric RP/MeOH	Plasma (100 µL)	HPLC-ESI-TripleTOF	[142]
Bile acids and derivatives					
	OPE	Methanol	Rat serum (10 µL)	UPLC-ESI-QTRAP/QTOF	[143]

Table 3. *Cont.*

Lipid Class	Extraction Method	System	Biological Matrix (Sample Amount)	Platform	Ref
	A. OPE or D. LLE	A. ACN; D: ACN - 400 g/L NH_4SO_4 - H_2O (1:1:0.35)	Serum (100 µL)	HPLC-ESI-QqQ	[144]
	PD-SPE	Ostro 96 well plates/cold ACN with 1% of FA	Plasma-Serum (100 µL)	UHPLC-ESI-QqQ	[145]
	SPE	*i*PrOH/Polymeric RP/MeOH - 0.02% FA (10:90)	Plasma-Serum-CSF (100 µL)	HPLC-ESI-QTRAP	[134]
	OPE	iPrOH	Feces (1 g)	HPLC-ESI-QqQ	[146]
	1. OPE, 2. SPE	1. Saline solution - (60 °C) Ethanol (1:1); 2. Extract - H2O (1:10)/Polymeric RP/MeOH	Rat brain tissue (1.5–1.8 g)	HPLC-ESI-QqQ	[147]
Prenol lipids					
Isoprenoids					
	LLE	Et_2O - PBS (pH = 7.4) - EtOH (1:1:0.2)	Feces (0.3–0.5 g)	HPLC-DAD	[148]
	OPE	ACN - MeOH - H_2O (2:1:1)	Natural rubber (1.5 g)	HPLC-ESI-QqQ	[149]
	OPE	Methanol - H_2O (1:1)	Bacterial cells (1.5 mL, OD: 5)	HPLC-ESI-TOF	[150]
	OPE	Methanol - H_2O (1:3)	Bacterial supernatant (1.5 mL)	HPLC-ESI-TOF	[150]
	OPE	*i*PrOH - 100 mM NH_4HCO_3 (pH 7.4) (1:1)	Human cells	UPLC-ESI-QqQ	[151]
	SPE	2% FA/Polymeric RP/Hex - *i*PrOH - NH_4OH (12:7:1)	Plasma (300 µL)	UPLC-ESI-QqQ	[151]
Quinones and hydroquinones					
	LLE	Saturated K_2CO_3 - CH_2Cl_2 (1:1)	Urine (Rats: 2 mL Human: 10 mL)	GC-Q	[152]
	LLE	$CHCl_3$ - MeOH (3:7) - cold 10% NaCl + BHT	Bacterial cells (10–50 mg)	HPLC-APCI-QTRAP	[153]
Saccharolipids					
Acylaminosugars					
	1. LLE, 2. LLE	1. 45% Phenol - H_2O; 2. $CHCl_3$ - MeOH - H_2O (2:1:3) + Deriv. aq phase.	Bacterial cells (2 g/mL)	GC-Q	[154]

Table 3. *Cont.*

Lipid Class	Extraction Method	System	Biological Matrix (Sample Amount)	Platform	Ref
	LLE	50% Phenol - H_2O	Acetone-dried bacteria	UHPLC-ESI-QTOF	[155]
	SPE	Genlantis SoluLyse detergent/AEC/5% NH_4OH in MeOH	Supernatant cell lysate (2×900 µL)	UPLC-ESI-QTRAP	[156]
Polyketides					
Linear polyketides					
	LLE	EtOAc	Bacterial supernatant (10 mL)	HPLC-ESI-LTQ-Orbitrap	[157]
	OPE	Acetone - MeOH (1:1)	Bacterial cells (10 mL culture)	HPLC-ESI-LTQ-Orbitrap	[157]
	OPE	MeOH	Bacterial supernatant (10 mL)	UPLC-ESI-QTOF	[158]
Aromatic polyketides					
	LLE	EtOAc + 1% HCl	Enzymatic mixture (500 µL)	HPLC-ESI-LTQ-Orbitrap	[159]
Flavonoids					
	OPE	70% MeOH + 3% FA	Digested cooked flour (1 mL)	UHPLC-HESI-QTRAP	[160]
	LLE	EtOAc	Blood-Tissue (50 µL)	UFLC-ESI-QqQ	[161, 162]
Polyether antibiotics					
	1. OPE, 2. OPE, 3. LLE, 4. SPE	1. MeOH; 2. 80% PrOH; 3. EtOAc - H_2O (1:1); 4. aq. phase/C18/80% PrOH	Microalga cells pellet (125–150 mL culture)	UPLC-nanoESI-QTOF	[163]

Table 3. *Cont.*

Lipid Class	Extraction Method	System	Biological Matrix (Sample Amount)	Platform	Ref
Annonaceae acetogenins					
	1. OPE, 2. LLE	1. Acetone; 2. CH_2Cl_2 - H_2O (1:1)	Avocado mesocarp (2g)-cotyledons (1g)	HPLC-ESI-TOF	[164]

AcCl: Acetyl chloride, Ace: Acetone, ACN: Acetonitrile, AcOH: Acetic acid, AEC: Anion exchange cartridge, AMPP: N-[4-(aminomethyl)phenyl]pyridinium, APCI: Atmospheric pressure chemical ionization, API: Atmospheric pressure ionization, aq.: aqueous, BHT: Butylated hydroxytoluene, BHT: Butylhydroxytoluene, BSTFA: N,O-Bis(trimethylsilyl)trifluoroacetamide, ButOH: n-Butanol, CA: Citric acid, Conc.: Concentration, CSF: cerebrospinal fluid, DAD: Diode Array Detection, DEA: Diethylamine, Deriv.: Derivatization, Diat.: Diatomaceous, DI: direct-infusion, DMAP: N,N-dimethylpyridin-4-amine, DMED: N,N-dimethylethylenediamine, DMG: N,N-dimethylglycine, DMTMM: 4-(4, 6-Dimethoxy-1,3,5-triazin-2-yl)-4-methylmorpholinium chloride, DnsHz: Dansylhydrazine, DTE: Dithioerythritol, EDTA: Ethylenediaminetetraacetic acid, EGTA: ethylene glycol-bis(β-aminoethyl ether)-N,N,N′,N′-tetraacetic acid, eq.: Equivalent, Et_2O: Diethyl ether, ESI: Electrospray ionization, EtOAc: Ethyl acetate, FA: Formic acid, FIA: Flow Injection Analysis, FT-ICR MS: Fourier transform ion cyclotron resonance mass spectrometry, HESI: Heated electrospray ionization mode, Hex: n-Hexane, iOct: 2,2,4-trimethylpentane (isooctane), iPrOH: 2-propanol, LLE: Liquid–liquid Extraction, LTQ: Linear Trap Quadrupole, MeONa: Sodium methoxide, MF: Methyl formate, MSTFA: N-Methyl-N-trimethylsilyl-trifluoracetamide, MTBE: Methyl tert-butyl ether, nanoESI: nano electrospray ionization, NH_4OAc: Ammonium acetate, NP: Normal phase, NPB: 3-nitrophenylboronic acid, OPE: One Phase Extraction, PAEA: 2-(2-Pyridilamino)-ethylamine, PBS: Phosphate Buffered Saline, PC: Protein content, PD-SPE: Phospholipid depletion solid phase extraction, PGWAT: Perigonadal white adipose tissue, PP: Potassium Phosphate, PrOH: 1-propanol, Q: Quadrupole, RP: Reverse Phase, SLE: Supported Liquid Extraction, SPE: Solid Phase Extraction, TFA: Trifluoroacetic acid, TOF: Time of flight, Tris-HCl: Tris(hydroxymethyl)aminomethane hydrochloride, UFLC: Ultra Fast Liquid Chromatography, μChip-SPE: Microchip-based SPE, μHP-SPE: micro-preparative high-performance solid-phase extraction. References were selected for studies conducted during the 2011–2020 period.

3.1. Glycerolipids (GL)

GL are neutral lipids composed of one glycerol backbone attached to at least one FA via ether or ester linkage. Structural classification is mainly based on the number of FA bound. Mono-, di-, and triradylglycerols are typically extracted with apolar organic solvents, including octane, cyclohexane, and MTBE. An alternative approach includes supercritical CO_2 for high-throughput separation of GL [165]. Pure chloroform and mixtures with methanol have also been reported [84,104,106,108]. Selective isolation of these hydrophobic species is achieved with low degradation, under mild conditions used in the extraction and minor reactivity of GL. Glycosylglycerols are another important subgroup in this class, which are characterized by sugar residues linked to the backbone. BD and Folch methods have been reported for the analysis of glycosylglycerols, such as digalactosyldiacylglycerols [110] and seminolipids [166].

3.2. Sphingolipids (SP)

The common backbone in SP consists of an amino alcohol, known as sphingoid base. Structural diversity arises from different chemical moieties linked to the amino and hydroxy groups. Important members of this family include ceramides, phosphospingolipids, cerebosides, and gangliosides. An up-to-date review by Montefusco et al. summarizes several experimental considerations for quantitative and qualitative analysis of sphingolipids [167]. In general, reports are consistent in comparable SP recoveries using chloroform-methanol-based and MTBE methods, with electrospray (ESI) as ionization source in positive and negative modes [21,23,62]. Mild alkaline and acidic extraction has also been combined with classic LLE protocols. Addition of MeONa [125] and KOH [126] has shown improved recovery and reproducibility in SP extraction, particularly ceramides and phosphosphingolipids. A standardized protocol for SP profiling is proposed by Sullards et al. [126]. For gangliosides, a quantitative approach involves derivatization using 4-(4, 6-Dimethoxy-1, 3, 5-triazin-2-yl)-4-methylmorpholinium chloride (DMTMM) and 2-(2-Pyridilamino)-ethylamine (PAEA) after protein precipitation [131]. The addition of a pyridylamine group increases the ionization efficiency resulting in a 15-fold signal intensity when compared to previously reported methods.

3.3. Glycerophospholipids (GP)

GP basic structure contains a glycerol base linked to one or two FA at the sn-1 and sn-2 positions. A phosphate group is also attached to the sn-3 position. Different bonding (acyl-, alkyl-, or alkenyl), length and unsaturation of the FAs create a wide range of combinations. However, GP are commonly subclassified based on the head group attached to the phosphate. Neutral phosphatidylcholine (PC) and phosphatidylethanolamine (PE) species, and charged ones including phosphatidic acid (PA), phosphatidylglycerol (PG), phosphatidylinositol (PI), phosphatidylserine (PS) and cardiolipins (CL) have precise locations and functions within cell membranes [168]. Most of neutral GP are successfully extracted with traditional procedures using chloroform or MTBE with comparable yields, except for LPCs [21,169]. For polar GPs like PI and LPA acidic conditions (pH 4–6) during extraction are recommended [170]. Tris or citric acid buffers are preferred for this purpose to avoid hydrolysis and interconversion of GP [119]. OPE protocols have also shown improved recoveries in polar GP, particularly PG and PS [23]. As alternative, specific SPE cartridges are commercially available for deproteinization and phospholipid preconcentration, such as HybridSPE-Phospholipid Ultra cartridge® [171] and iSPE®, with reported capability to isolate low-abundant GP [169,172,173].

3.4. Sterol Lipids (ST)

The structural skeleton of ST is based on a four fused ring. Differences in conjugation and position/type of polar functional groups generate a broad spectrum of polarities in this family. Lipid analysis in mammalian systems have focused on steroids, cholesterol and bile acids, while plants systems focus on phytosterols and phytostanols. Thin layer chromatography–flame ionization (TLC-FID) and

GC-MS techniques were initially used to determine ST with the requirement of derivatization (e.g., trimethylsilation and methylation). Nonetheless, an increasing number of publications have been implemented LC-MS strategies, since ST analysis can be performed in native state. Commonly, PPT or LLE methods are used for lipid extraction prior SPE in order to avoid interferences and signal suppression. Appropriate SPE elution solvents can resolve cholesterol from derivates like oxysterols and steroids given the differences in number of hydroxyl groups attached to the core ring. Moreover, antioxidants and metal chelators are commonly added to prevent ST oxidation during the extraction procedure [174]. For ST in plants, n-hexane and supercritical CO_2 have shown the best yields when combined with mechanical forces [175]. If esterified ST are targeted, a saponification stage under mild conditions can be included to remove fatty acyl groups without generation of artifacts [176].

3.5. Fatty Acyls (FA)

The structure of FA contains repeated series of methylene groups, derived from successive additions of malonyl-CoA or methylmalonyl-CoA to an acetyl-CoA primer. Differences in carbon chain lengths, degree of oxidation, unsaturation, and cyclations are the main sources of structural diversity. Major subclasses include fatty acids, fatty esters, and eicosanoids. Fatty acids have been traditionally derivatized for characterization by GC–MS. However, LC-MS and SFC-MS approaches provide quantitative signals for most fatty acids in biological samples. This allows the use of faster and milder conditions during lipid extraction, like BD and MTBE protocols. For extraction of eicosanoids, further measurements must be taken to avoid lipid degradation and artifact generation. Cold conditions (4 °C) and addition of antioxidants (e.g., BHT, BHA) are commonly introduced to preserve FA integrity within a sample. In a recent review on oxylipin extraction, Liakh et al. contrast PPT, LLE, and SPE methods. A combination of LLE previous SPE seems to be the best approach for preconcentration of oxylipins and other related species [177].

3.6. Prenol Lipids (PR)

PR carbon backbones comprise one or more isoprene units condensed. The number of terpene units and oxidation state of the structure form the basis of their classification. Isoprenoids, quinones and polyprenols are representative members of this class. Besides the well-known derivatization for GC-MS analysis of PR [178], recent OPE and LLE have been introduced for LC-MS methods. One-phase solvent systems containing diethyl ether, methanol, propanol and water are generally employed for the extraction, due to the relative polar character of PR in comparison to other bulk lipid classes. For higher yields of apolar PR like carotenoinds and tocopherols, either hexane or chloroform is added [148,179]. Supercritical fluids have also shown potential to efficiently extract and separate these compounds as reported in food and human serum studies [180]. Given their physicochemical similarities, ST are commonly co-extracted with PR, even after saponification. However, conventional ST precipitation with petroleum ether [181] or SPE enrichment [151] could be used to achieve separation of PRs. Additionally, extraction conditions such as neutral or slightly basic pH, presence of antioxidants and absence of light improve extraction yield and minimize PR degradation.

3.7. Polyketides (PK)

PK are a structural diverse lipid class derived from sequential condensations of ketoacyl groups. PK are characterized by backbones with at least two carbonyls linked by a carbon atom, and also subject to functional modifications including hydroxylation, glycosylation, methylation among others. Further subclassification include macrolides, aromatic polyketides, and flavonoids. The abundance of polar groups and double bounds in PK structures allow the use of polar solvents to narrow down the type of lipids to be extracted. Targeted studies report either ethyl acetate or methanol as OPE solvents. Considering that plants, fungi, and bacteria are the main biological sources of PK, mechanical forces are commonly applied during the extraction. Pressurized systems with [182] or without [183] supercritical fluids increase significantly the PK recovery. SPE methods have also been adopted for

PK fractionation and preconcentration using reverse phase cartridges (e.g., Strata™-X(Torrance, CA 90501-1430, USA), Sep-Pak Plus C18), particularly for prymnesins [163] and flavonoids [184]. Other important parameters must be optimized for the extraction, including sample amount, sample-solvent ratio and temperature. Finally, extraction of PK prone to oxidation (e.g., polyphenols) can incorporate β-mercaptoethanol or $K_2S_2O_5$ to decrease unwanted redox processes.

3.8. Saccharolipids (SL)

SL are distinguished by a sugar backbone linked to FAs via glycosidic bonds. Representative members of this class include lipopolysaccharides (LPS) synthesized by gram-negative bacteria. Several methods have been developed for LPS extraction based on the analytical technique for detection and quantification. For MS studies, phenol-based methods are the standard for SL extraction, including hot phenol extraction (HPE), aqueous phenol-chloroform and aqueous phenol-diethyl ether extraction [185]. Recently, alternative at-room-temperature protocols have been tested to improve efficiency, yield, and lipid integrity. SPE [156] and methanol-chloroform [155] methods are reported in cell membrane characterizations.

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4. Conclusions and Future Perspectives

The high-throughput analysis of lipids using mass spectrometry provides a snapshot into complex lipidomes in living organisms. However, lipid identification and quantification are limited by the selected extraction protocol. Structural features not only drive the intermolecular interactions within an extraction system, but also dictates their stability and reactivity. Furthermore, type and amount of biological matrix should be well considered for protocol selection and validation. Despite the efforts of several researchers, the lack of standardized procedures for sample preparation in lipidomics is still a major concern in the field. Therefore, comparative studies contrasting two or more different isolations techniques, along with inclusion of extraction protocols in lipid databases, provide valuable insights and criterion.

Preservation of lipidome integrity must be prioritized through extraction procedures, otherwise lipid extracts would not faithfully retain biological variations and comparisons across samples will be inaccurate. Automatized lipid isolation represents a feasible solution by taking advantage of simple and versatile protocols. Although not all samples are suitable subjects of automatization, advances in SPME-LC online interfaces and combined extraction of amphiphilic and lipophilic compounds in glass-coated microplates are promising.

For untargeted approaches, the main limitations are the narrow coverage and differential yield of extracted lipid species. Meanwhile, repeatability and reproducibility through several extraction steps are constraints faced by targeted approaches. Future lipidomic studies will account for lipid sub-cellular localization, interaction with physiological partners and monitor concentrations changes over time using fast, reproducible, and versatile extraction protocols to assure an accurate depiction of the dynamic changes taking place in biological systems.

Author Contributions: Conceptualization, J.A. and M.P.C.; literature review, J.A., A.R.-O. and M.P.C.; writing—review and editing J.A and M.P.C. All authors accepted the final version of the review. All authors have read and agreed to the published version of the manuscript.

Funding: The APC was funded by Metabolomics Core Facility-MetCore at the Univerisidad de Los Andes a facility that is supported by the vicepresidency for research.

Conflicts of Interest: The authors declare no conflict of interest.

References

1. Fahy, E.; Subramaniam, S.; Brown, H.A.; Glass, C.K.; Merrill, A.H.; Murphy, R.C.; Raetz, C.R.H.; Russell, D.W.; Seyama, Y.; Shaw, W.; et al. A Comprehensive Classification System for Lipids. *J. Lipid Res.* **2005**, *46*, 839–862. [CrossRef] [PubMed]
2. Fahy, E.; Subramaniam, S.; Murphy, R.C.; Nishijima, M.; Raetz, C.R.H.; Shimizu, T.; Spener, F.; Meer, G.; van Wakelam, M.J.O.; Dennis, E.A. Update of the LIPID MAPS Comprehensive Classification System for Lipids. *J. Lipid Res.* **2009**, *50*, S9–S14. [CrossRef] [PubMed]
3. Fahy, E.; Cotter, D.; Sud, M.; Subramaniam, S. Lipid Classification, Structures and Tools. *Biochim. Biophys. Acta - Mol. Cell Biol. Lipids* **2011**, *1811*, 637–647. [CrossRef] [PubMed]
4. Han, X.; Gross, R.W. Shotgun Lipidomics: Electrospray Ionization Mass Spectrometric Analysis and Quantitation of Cellular Lipidomes Directly from Crude Extracts of Biological Samples. *Mass Spectrom. Rev.* **2005**, *24*, 367–412. [CrossRef]
5. Van Meer, G.; de Kroon, A.I.P.M. Lipid Map of the Mammalian Cell. *J. Cell Sci.* **2011**, *124*, 5–8. [CrossRef]
6. Watson, A.D. Lipidomics: A Global Approach to Lipid Analysis in Biological Systems. *J. Lipid Res.* **2006**, *47*, 2101–2111. [CrossRef]
7. Wong, M.W.; Braidy, N.; Poljak, A.; Pickford, R.; Thambisetty, M.; Sachdev, P.S. Dysregulation of Lipids in Alzheimer's Disease and Their Role as Potential Biomarkers. *Alzheimer's Dement. J. Alzheimer's Assoc.* **2017**, *13*, 810–827. [CrossRef]
8. Perrotti, F.; Rosa, C.; Cicalini, I.; Sacchetta, P.; Del Boccio, P.; Genovesi, D.; Pieragostino, D. Advances in Lipidomics for Cancer Biomarkers Discovery. *Int. J. Mol. Sci.* **2016**, *17*, 1992. [CrossRef]
9. Mika, A.; Sledzinski , T.; Stepnowski, P. Current Progress of Lipid Analysis in Metabolic Diseases by Mass Spectrometry Methods. *Curr. Med. Chem.* **2019**, 60–103. [CrossRef]
10. Tenenboim, H.; Burgos, A.; Willmitzer, L.; Brotman, Y. Using Lipidomics for Expanding the Knowledge on Lipid Metabolism in Plants. *Biochimie* **2016**, *130*, 91–96. [CrossRef]
11. Appala, K.; Bimpeh, K.; Freeman, C.; Hines, K.M. Recent Applications of Mass Spectrometry in Bacterial Lipidomics. *Anal. Bioanal. Chem.* **2020**. [CrossRef] [PubMed]
12. Hewelt-Belka, W.; Nakonieczna, J.; Belka, M.; Bączek, T.; Namieśnik, J.; Kot-Wasik, A. Untargeted Lipidomics Reveals Differences in the Lipid Pattern among Clinical Isolates of Staphylococcus Aureus Resistant and Sensitive to Antibiotics. *J. Proteome Res.* **2016**, *15*, 914–922. [CrossRef] [PubMed]
13. Wang, J.; Wang, C.; Han, X. Tutorial on Lipidomics. *Anal. Chim. Acta* **2019**, *1061*, 28–41. [CrossRef] [PubMed]
14. Cajka, T.; Fiehn, O. Comprehensive Analysis of Lipids in Biological Systems by Liquid Chromatography-Mass Spectrometry. *TrAC Trends Anal. Chem.* **2014**, *61*, 192–206. [CrossRef] [PubMed]
15. Cajka, T.; Fiehn, O. Toward Merging Untargeted and Targeted Methods in Mass Spectrometry-Based Metabolomics and Lipidomics. *Anal. Chem.* **2016**, *88*, 524–545. [CrossRef]
16. Folch, J.; Lees, M.; Stanley, G.H.S. A simple method for the isolation and purification of total lipides from animal tissues. *J. Biol. Chem.* **1957**, *226*, 497–509.
17. Bligh, E.G.; Dyer, W.J. A rapid method of total lipid extraction and purification. *Can. J. Biochem. Physiol.* **1959**, *37*, 911–917. [CrossRef]
18. Matyash, V.; Liebisch, G.; Kurzchalia, T.V.; Shevchenko, A.; Schwudke, D. Lipid Extraction by Methyl-Tert-Butyl Ether for High-Throughput Lipidomics. *J. Lipid Res.* **2008**, *49*, 1137–1146. [CrossRef]
19. Löfgren, L.; Ståhlman, M.; Forsberg, G.-B.; Saarinen, S.; Nilsson, R.; Hansson, G.I. The BUME Method: A Novel Automated Chloroform-Free 96-Well Total Lipid Extraction Method for Blood Plasma. *J. Lipid Res.* **2012**, *53*, 1690–1700. [CrossRef]
20. Sostare, J.; Di Guida, R.; Kirwan, J.; Chalal, K.; Palmer, E.; Dunn, W.B.; Viant, M.R. Comparison of Modified Matyash Method to Conventional Solvent Systems for Polar Metabolite and Lipid Extractions. *Anal. Chim. Acta* **2018**, *1037*, 301–315. [CrossRef]

21. Ulmer, C.Z.; Jones, C.M.; Yost, R.A.; Garrett, T.J.; Bowden, J.A. Optimization of Folch, Bligh-Dyer, and Matyash Sample-to-Extraction Solvent Ratios for Human Plasma-Based Lipidomics Studies. *Anal. Chim. Acta* **2018**, *1037*, 351–357. [CrossRef] [PubMed]
22. Satomi, Y.; Hirayama, M.; Kobayashi, H. One-Step Lipid Extraction for Plasma Lipidomics Analysis by Liquid Chromatography Mass Spectrometry. *J. Chromatogr. B* **2017**, *1063*, 93–100. [CrossRef] [PubMed]
23. Sarafian, M.H.; Gaudin, M.; Lewis, M.R.; Martin, F.-P.; Holmes, E.; Nicholson, J.K.; Dumas, M.-E. Objective Set of Criteria for Optimization of Sample Preparation Procedures for Ultra-High Throughput Untargeted Blood Plasma Lipid Profiling by Ultra Performance Liquid Chromatography–Mass Spectrometry. *Anal. Chem.* **2014**, *86*, 5766–5774. [CrossRef] [PubMed]
24. Zein Elabdeen, H.R.; Mustafa, M.; Szklenar, M.; Rühl, R.; Ali, R.; Bolstad, A.I. Ratio of Pro-Resolving and Pro-Inflammatory Lipid Mediator Precursors as Potential Markers for Aggressive Periodontitis. *PLoS ONE* **2013**, *8*, e70838. [CrossRef]
25. Jurowski, K.; Kochan, K.; Walczak, J.; Barańska, M.; Piekoszewski, W.; Buszewski, B. Comprehensive Review of Trends and Analytical Strategies Applied for Biological Samples Preparation and Storage in Modern Medical Lipidomics: State of the Art. *TrAC Trends Anal. Chem.* **2017**, *86*, 276–289. [CrossRef]
26. Zhang, S.; Liu, L.; Steffen, D.; Ye, T.; Raftery, D. Metabolic Profiling of Gender: Headspace-SPME/GC–MS and 1H NMR Analysis of Urine. *Metabolomics* **2012**, *8*, 323–334. [CrossRef]
27. Silva, C.L.; Passos, M.; Câmara, J.S. Solid Phase Microextraction, Mass Spectrometry and Metabolomic Approaches for Detection of Potential Urinary Cancer Biomarkers—A Powerful Strategy for Breast Cancer Diagnosis. *Talanta* **2012**, *89*, 360–368. [CrossRef]
28. Pawliszyn, J. Theory of Solid-Phase Microextraction. *J. Chromatogr. Sci.* **2000**, *38*, 270–278. [CrossRef]
29. Wang, M.; Wang, C.; Han, R.H.; Han, X. Novel Advances in Shotgun Lipidomics for Biology and Medicine. *Prog. Lipid Res.* **2016**, *61*, 83–108. [CrossRef]
30. Reichardt, C.; Welton, T.; Appendix, A. Properties, Purification, and Use of Organic Solvents. In *Solvents and Solvent Effects in Organic Chemistry*; Wiley: Hoboken, NJ, USA, 2010; pp. 549–586. [CrossRef]
31. Seyer, A.; Boudah, S.; Broudin, S.; Junot, C.; Colsch, B. Annotation of the Human Cerebrospinal Fluid Lipidome Using High Resolution Mass Spectrometry and a Dedicated Data Processing Workflow. *Metabolomics* **2016**, *12*, 91. [CrossRef]
32. Burla, B.; Arita, M.; Arita, M.; Bendt, A.K.; Cazenave-Gassiot, A.; Dennis, E.A.; Ekroos, K.; Han, X.; Ikeda, K.; Liebisch, G.; et al. MS-Based Lipidomics of Human Blood Plasma—A Community-Initiated Position Paper to Develop Accepted Guidelines. *J. Lipid Res.* **2018**. [CrossRef] [PubMed]
33. Van Meulebroek, L.; De Paepe, E.; Vercruysse, V.; Pomian, B.; Bos, S.; Lapauw, B.; Vanhaecke, L. Holistic Lipidomics of the Human Gut Phenotype Using Validated Ultra-High-Performance Liquid Chromatography Coupled to Hybrid Orbitrap Mass Spectrometry. *Anal. Chem.* **2017**, *89*, 12502–12510. [CrossRef] [PubMed]
34. Wong, M.W.K.; Braidy, N.; Pickford, R.; Sachdev, P.S.; Poljak, A. Comparison of Single Phase and Biphasic Extraction Protocols for Lipidomic Studies Using Human Plasma. *Front. Neurol.* **2019**, *10*, 879. [CrossRef]
35. Gardner, M.S.; Kuklenyik, Z.; Lehtikoski, A.; Carter, K.A.; McWilliams, L.G.; Kusovschi, J.; Bierbaum, K.; Jones, J.I.; Rees, J.; Reis, G.; et al. Development and Application of a High Throughput One-Pot Extraction Protocol for Quantitative LC-MS/MS Analysis of Phospholipids in Serum and Lipoprotein Fractions in Normolipidemic and Dyslipidemic Subjects. *J. Chromatogr. B* **2019**, *1118–1119*, 137–147. [CrossRef]
36. Shibusawa, Y.; Yamakawa, Y.; Noji, R.; Yanagida, A.; Shindo, H.; Ito, Y. Three-Phase Solvent Systems for Comprehensive Separation of a Wide Variety of Compounds by High-Speed Counter-Current Chromatography. *J. Chromatogr. A* **2006**, *1133*, 119–125. [CrossRef] [PubMed]
37. Leopold, J.; Popkova, Y.; Engel, K.M.; Schiller, J. Recent Developments of Useful MALDI Matrices for the Mass Spectrometric Characterization of Lipids. *Biomolecules* **2018**, *8*, 173. [CrossRef]
38. Alshehry, H.Z.; Barlow, K.C.; Weir, M.J.; Zhou, Y.; McConville, J.M.; Meikle, J.P. An Efficient Single Phase Method for the Extraction of Plasma Lipids. *Metabolites* **2015**, *5*, 389. [CrossRef]
39. Alshehry, Z.H.; Mundra, P.A.; Barlow, C.K.; Mellett, N.A.; Wong, G.; McConville, M.J.; Simes, J.; Tonkin, A.M.; Sullivan, D.R.; Barnes, E.H.; et al. Plasma Lipidomic Profiles Improve on Traditional Risk Factors for the Prediction of Cardiovascular Events in Type 2 Diabetes Mellitus. *Circulation* **2016**, *134*, 1637–1650. [CrossRef]

40. Meikle, P.J.; Gerard, W.; Despina, T.; Barlow, C.K.; Weir, J.M.; Christopher, M.J.; MacIntosh, G.L.; Benjamin, G.; Linda, S.; Adam, K.; et al. Plasma Lipidomic Analysis of Stable and Unstable Coronary Artery Disease. *Arterioscler. Thromb. Vasc. Biol.* **2011**, *31*, 2723–2732. [CrossRef]
41. Iriondo, A.; Tainta, M.; Saldias, J.; Arriba, M.; Ochoa, B.; Goñi, F.M.; Martinez-Lage, P.; Abad-García, B. Isopropanol Extraction for Cerebrospinal Fluid Lipidomic Profiling Analysis. *Talanta* **2019**, *195*, 619–627. [CrossRef] [PubMed]
42. Rombouts, C.; De Spiegeleer, M.; Van Meulebroek, L.; De Vos, W.H.; Vanhaecke, L. Validated Comprehensive Metabolomics and Lipidomics Analysis of Colon Tissue and Cell Lines. *Anal. Chim. Acta* **2019**, *1066*, 79–92. [CrossRef] [PubMed]
43. Birjandi, A.P.; Bojko, B.; Ning, Z.; Figeys, D.; Pawliszyn, J. High Throughput Solid Phase Microextraction: A New Alternative for Analysis of Cellular Lipidome? *J. Chromatogr. B* **2017**, *1043*, 12–19. [CrossRef]
44. Astarita, G.; Ahmed, F.; Piomelli, D. *Lipidomic Analysis of Biological Samples by Liquid Chromatography Coupled to Mass Spectrometry BT—Lipidomics: Volume 1: Methods and Protocols*; Armstrong, D., Ed.; Humana Press: Totowa, NJ, USA, 2009; pp. 201–219. [CrossRef]
45. Shi, C.; Guo, H.; Wu, T.; Tao, N.; Wang, X.; Zhong, J. Effect of Three Types of Thermal Processing Methods on the Lipidomics Profile of Tilapia Fillets by UPLC-Q-Extractive Orbitrap Mass Spectrometry. *Food Chem.* **2019**, *298*, 125029. [CrossRef] [PubMed]
46. Yu, Z.; Xiang, X.; Jin, Y.; Wang, N.; Ma, M. High-Throughput Lipidomic Profiling of High-Density Lipoprotein from Egg Yolk (EYHDL): Comparison Based on UPLC-MS/MS and GC–MS. *Eur. Food Res. Technol.* **2019**, *245*, 1665–1675. [CrossRef]
47. Chen, J.; Nichols, K.K.; Wilson, L.; Barnes, S.; Nichols, J.J. Untargeted Lipidomic Analysis of Human Tears: A New Approach for Quantification of O-Acyl-Omega Hydroxy Fatty Acids. *Ocul. Surf.* **2019**, *17*, 347–355. [CrossRef]
48. Martins-Noguerol, R.; Moreno-Pérez, J.A.; Acket, S.; Makni, S.; Garcés, R.; Troncoso-Ponce, A.; Salas, J.J.; Thomasset, B.; Martínez-Force, E. Lipidomic Analysis of Plastidial Octanoyltransferase Mutants of Arabidopsis Thaliana. *Metabolites* **2019**, *9*, 209. [CrossRef]
49. Min, H.K.; Lim, S.; Chung, B.C.; Moon, M.H. Shotgun Lipidomics for Candidate Biomarkers of Urinary Phospholipids in Prostate Cancer. *Anal. Bioanal. Chem.* **2011**, *399*, 823–830. [CrossRef]
50. Gregory, K.E.; Bird, S.S.; Gross, V.S.; Marur, V.R.; Lazarev, A.V.; Walker, W.A.; Kristal, B.S. Method Development for Fecal Lipidomics Profiling. *Anal. Chem.* **2013**, *85*, 1114–1123. [CrossRef] [PubMed]
51. Löfgren, L.; Forsberg, G.-B.; Ståhlman, M. The BUME Method: A New Rapid and Simple Chloroform-Free Method for Total Lipid Extraction of Animal Tissue. *Sci. Rep.* **2016**, *6*, 27688. [CrossRef] [PubMed]
52. Carrizo, D.; Nerín, I.; Domeño, C.; Alfaro, P.; Nerín, C. Direct Screening of Tobacco Indicators in Urine and Saliva by Atmospheric Pressure Solid Analysis Probe Coupled to Quadrupole-Time of Flight Mass Spectrometry (ASAP-MS-Q-TOF-). *J. Pharm. Biomed. Anal.* **2016**, *124*, 149–156. [CrossRef] [PubMed]
53. Burgos, A.; Szymanski, J.; Seiwert, B.; Degenkolbe, T.; Hannah, M.A.; Giavalisco, P.; Willmitzer, L. Analysis of Short-Term Changes in the Arabidopsis Thaliana Glycerolipidome in Response to Temperature and Light. *Plant J.* **2011**, *66*, 656–668. [CrossRef] [PubMed]
54. Okazaki, Y.; Kamide, Y.; Hirai, M.Y.; Saito, K. Plant Lipidomics Based on Hydrophilic Interaction Chromatography Coupled to Ion Trap Time-of-Flight Mass Spectrometry. *Metabolomics* **2013**, *9*, 121–131. [CrossRef] [PubMed]
55. Cala, M.P.; Aldana, J.; Medina, J.; Sánchez, J.; Guio, J.; Wist, J.; Meesters, R.J.W. Multiplatform Plasma Metabolic and Lipid Fingerprinting of Breast Cancer: A Pilot Control-Case Study in Colombian Hispanic Women. *PLoS ONE* **2018**, *13*, e0190958. [CrossRef]
56. Cala, M.; Aldana, J.; Sánchez, J.; Guio, J.; Meesters, R.J.W. Urinary Metabolite and Lipid Alterations in Colombian Hispanic Women with Breast Cancer: A Pilot Study. *J. Pharm. Biomed. Anal.* **2018**, *152*, 234–241. [CrossRef]
57. Navarro-Reig, M.; Tauler, R.; Iriondo-Frias, G.; Jaumot, J. Untargeted Lipidomic Evaluation of Hydric and Heat Stresses on Rice Growth. *J. Chromatogr. B* **2019**, *1104*, 148–156. [CrossRef]
58. Villaseñor, A.; Garcia-Perez, I.; Garcia, A.; Posma, J.M.; Fernández-López, M.; Nicholas, A.J.; Modi, N.; Holmes, E.; Barbas, C. Breast Milk Metabolome Characterization in a Single-Phase Extraction, Multiplatform Analytical Approach. *Anal. Chem.* **2014**, *86*, 8245–8252. [CrossRef] [PubMed]

59. Hummel, J.; Segu, S.; Li, Y.; Irgang, S.; Jueppner, J.; Giavalisco, P. Ultra Performance Liquid Chromatography and High Resolution Mass Spectrometry for the Analysis of Plant Lipids. *Front. Plant Sci.* **2011**, *2*, 54. [CrossRef]
60. Ali, A.S.; Raju, R.; Ray, S.; Kshirsagar, R.; Gilbert, A.; Zang, L.; Karger, B.L. Lipidomics of CHO Cell Bioprocessing: Relation to Cell Growth and Specific Productivity of a Monoclonal Antibody. *Biotechnol. J.* **2018**, *13*, 1700745. [CrossRef]
61. Zhang, H.; Gao, Y.; Sun, J.; Fan, S.; Yao, X.; Ran, X.; Zheng, C.; Huang, M.; Bi, H. Optimization of Lipid Extraction and Analytical Protocols for UHPLC-ESI-HRMS-Based Lipidomic Analysis of Adherent Mammalian Cancer Cells. *Anal. Bioanal. Chem.* **2017**, *409*, 5349–5358. [CrossRef]
62. Calderón, C.; Sanwald, C.; Schlotterbeck, J.; Drotleff, B.; Lämmerhofer, M. Comparison of Simple Monophasic versus Classical Biphasic Extraction Protocols for Comprehensive UHPLC-MS/MS Lipidomic Analysis of Hela Cells. *Anal. Chim. Acta* **2019**, *1048*, 66–74. [CrossRef]
63. Nilsson, A.K.; Sjöbom, U.; Christenson, K.; Hellström, A. Lipid Profiling of Suction Blister Fluid: Comparison of Lipids in Interstitial Fluid and Plasma. *Lipids Health Dis.* **2019**, *18*, 164. [CrossRef] [PubMed]
64. Greenwood, D.J.; Dos Santos, M.S.; Huang, S.; Russell, M.R.G.; Collinson, L.M.; MacRae, J.I.; West, A.; Jiang, H.; Gutierrez, M.G. Subcellular Antibiotic Visualization Reveals a Dynamic Drug Reservoir in Infected Macrophages. *Science* **2019**, *364*, 1279–1282. [CrossRef] [PubMed]
65. Anand, S.; Barnes, J.M.; Young, S.A.; Garcia, D.M.; Tolley, H.D.; Kauwe, J.S.K.; Graves, S.W. Discovery and Confirmation of Diagnostic Serum Lipid Biomarkers for Alzheimer's Disease Using Direct Infusion Mass Spectrometry. *J. Alzheimer's Dis.* **2017**, *59*, 277–290.
66. Gulati, S.; Ekland, E.H.; Ruggles, K.V.; Chan, R.B.; Jayabalasingham, B.; Zhou, B.; Mantel, P.-Y.; Lee, M.C.S.; Spottiswoode, N.; Coburn-Flynn, O.; et al. Profiling the Essential Nature of Lipid Metabolism in Asexual Blood and Gametocyte Stages of Plasmodium Falciparum. *Cell Host Microbe* **2015**, *18*, 371–381. [CrossRef]
67. Uchikata, T.; Matsubara, A.; Fukusaki, E.; Bamba, T. High-Throughput Phospholipid Profiling System Based on Supercritical Fluid Extraction–Supercritical Fluid Chromatography/Mass Spectrometry for Dried Plasma Spot Analysis. *J. Chromatogr. A* **2012**, *1250*, 69–75. [CrossRef]
68. Lísa, M.; Holčapek, M. *UHPSFC/ESI-MS Analysis of Lipids BT—Clinical Metabolomics: Methods and Protocols*; Giera, M., Ed.; Springer: New York, NY, USA, 2018; pp. 73–82. [CrossRef]
69. Yang, Y.; Zhong, Q.; Zhang, H.; Mo, C.; Yao, J.; Huang, T.; Zhou, T.; Tan, W. Lipidomics Study of the Protective Effects of Isosteviol Sodium on Stroke Rats Using Ultra High-Performance Supercritical Fluid Chromatography Coupling with Ion-Trap and Time-of-Flight Tandem Mass Spectrometry. *J. Pharm. Biomed. Anal.* **2018**, *157*, 145–155. [CrossRef]
70. Bojko, B.; Wąsowicz, M.; Pawliszyn, J. Metabolic Profiling of Plasma from Cardiac Surgical Patients Concurrently Administered with Tranexamic Acid: DI-SPME–LC–MS Analysis. *J. Pharm. Anal.* **2014**, *4*, 6–13. [CrossRef]
71. Bessonneau, V.; Bojko, B.; Pawliszyn, J. Analysis of Human Saliva Metabolome by Direct Immersion Solid-Phase Microextraction LC and Benchtop Orbitrap MS. *Bioanalysis* **2013**, *5*, 783–792. [CrossRef]
72. Garwolińska, D.; Hewelt-Belka, W.; Namieśnik, J.; Kot-Wasik, A. Rapid Characterization of the Human Breast Milk Lipidome Using a Solid-Phase Microextraction and Liquid Chromatography–Mass Spectrometry-Based Approach. *J. Proteome Res.* **2017**, *16*, 3200–3208. [CrossRef]
73. Liu, X.; Zhou, L.; Shi, X.; Xu, G. New Advances in Analytical Methods for Mass Spectrometry-Based Large-Scale Metabolomics Study. *TrAC Trends Anal. Chem.* **2019**, *121*, 115665. [CrossRef]
74. Yang, Y.; Liang, Y.; Yang, J.; Ye, F.; Zhou, T.; Gongke, L. Advances of Supercritical Fluid Chromatography in Lipid Profiling. *J. Pharm. Anal.* **2019**, *9*, 1–8. [CrossRef] [PubMed]
75. Furse, S.; Egmond, M.R.; Killian, J.A. Isolation of Lipids from Biological Samples. *Mol. Membr. Biol.* **2015**, *32*, 55–64. [CrossRef] [PubMed]
76. Sethi, S.; Brietzke, E. Recent Advances in Lipidomics: Analytical and Clinical Perspectives. *Prostaglandins Other Lipid Mediat.* **2017**, *128–129*, 8–16. [CrossRef] [PubMed]
77. König, S.; Ischebeck, T.; Lerche, J.; Stenzel, I.; Heilmann, I. Salt-Stress-Induced Association of Phosphatidylinositol 4,5-Bisphosphate with Clathrin-Coated Vesicles in Plants. *Biochem. J.* **2008**, *415*, 387–399. [CrossRef]
78. Lubary, M.; Hofland, G.W.; ter Horst, J.H. A Process for the Production of a Diacylglycerol-Based Milk Fat Analogue. *Eur. J. Lipid Sci. Technol.* **2011**, *113*, 459–468. [CrossRef]

79. Schlotterbeck, J.; Cebo, M.; Kolb, A.; Lämmerhofer, M. Quantitative Analysis of Chemoresistance-Inducing Fatty Acid in Food Supplements Using UHPLC–ESI-MS/MS. *Anal. Bioanal. Chem.* **2019**, *411*, 479–491. [CrossRef]
80. Zhang, S.; Wang, H.; Zhu, M.-J. A Sensitive GC/MS Detection Method for Analyzing Microbial Metabolites Short Chain Fatty Acids in Fecal and Serum Samples. *Talanta* **2019**, *196*, 249–254. [CrossRef]
81. Pérez-Navarro, J.; Da Ros, A.; Masuero, D.; Izquierdo-Cañas, P.M.; Hermosín-Gutiérrez, I.; Gómez-Alonso, S.; Mattivi, F.; Vrhovsek, U. LC-MS/MS Analysis of Free Fatty Acid Composition and Other Lipids in Skins and Seeds of Vitis Vinifera Grape Cultivars. *Food Res. Int.* **2019**, *125*, 108556. [CrossRef]
82. Mehari, B.; Redi-Abshiro, M.; Chandravanshi, B.S.; Combrinck, S.; McCrindle, R.; Atlabachew, M. GC-MS Profiling of Fatty Acids in Green Coffee (*Coffea arabica* L.) Beans and Chemometric Modeling for Tracing Geographical Origins from Ethiopia. *J. Sci. Food Agric.* **2019**, *99*, 3811–3823. [CrossRef]
83. Zarai, Z.; Eddehech, A.; Rigano, F.; Oteri, M.; Micalizzi, G.; Dugo, P.; Mondello, L.; Cacciola, F. Characterization of Monoacylglycerols and Diacylglycerols Rich in Polyunsaturated Fatty Acids Produced by Hydrolysis of Musteleus Mustelus Liver Oil Catalyzed by an Immobilized Bacterial Lipase. *J. Chromatogr. A* **2020**, *1613*, 460692. [CrossRef]
84. Gašparović, B.; Penezić, A.; Lampitt, R.S.; Sudasinghe, N.; Schaub, T. Free Fatty Acids, Tri-, Di- and Monoacylglycerol Production and Depth-Related Cycling in the Northeast Atlantic. *Mar. Chem.* **2016**, *186*, 101–109. [CrossRef]
85. Jensen, J.R.; Pitcher, M.H.; Yuan, Z.X.; Ramsden, C.E.; Domenichiello, A.F. Concentrations of Oxidized Linoleic Acid Derived Lipid Mediators in the Amygdala and Periaqueductal Grey Are Reduced in a Mouse Model of Chronic Inflammatory Pain. *Prostaglandins, Leukot. Essent. Fat. Acids* **2018**, *135*, 128–136. [CrossRef] [PubMed]
86. Rund, K.M.; Ostermann, A.I.; Kutzner, L.; Galano, J.-M.; Oger, C.; Vigor, C.; Wecklein, S.; Seiwert, N.; Durand, T.; Schebb, N.H. Development of an LC-ESI(-)-MS/MS Method for the Simultaneous Quantification of 35 Isoprostanes and Isofurans Derived from the Major N3- and N6-PUFAs. *Anal. Chim. Acta* **2018**, *1037*, 63–74. [CrossRef]
87. Sanak, M.; Gielicz, A.; Nagraba, K.; Kaszuba, M.; Kumik, J.; Szczeklik, A. Targeted Eicosanoids Lipidomics of Exhaled Breath Condensate in Healthy Subjects. *J. Chromatogr. B* **2010**, *878*, 1796–1800. [CrossRef] [PubMed]
88. Miller, T.M.; Poloyac, S.M.; Anderson, K.B.; Waddell, B.L.; Messamore, E.; Yao, J.K. A Rapid UPLC-MS/MS Assay for Eicosanoids in Human Plasma: Application to Evaluate Niacin Responsivity. *Prostaglandins Leukot. Essent. Fat. Acids* **2018**, *136*, 153–159. [CrossRef] [PubMed]
89. Cummings, M.; Massey, K.A.; Mappa, G.; Wilkinson, N.; Hutson, R.; Munot, S.; Saidi, S.; Nugent, D.; Broadhead, T.; Wright, A.I.; et al. Integrated Eicosanoid Lipidomics and Gene Expression Reveal Decreased Prostaglandin Catabolism and Increased 5-Lipoxygenase Expression in Aggressive Subtypes of Endometrial Cancer. *J. Pathol.* **2019**, *247*, 21–34. [CrossRef]
90. Gobo, L.A.; de Carvalho, L.M.; Temp, F.; Viana, C.; Mello, C.F. A Rapid Method for Identification and Quantification of Prostaglandins in Cerebral Tissues by UHPLC-ESI-MS/MS for the Lipidomic in Vivo Studies. *Anal. Biochem.* **2018**, *545*, 98–103. [CrossRef]
91. Dumlao, D.S.; Buczynski, M.W.; Norris, P.C.; Harkewicz, R.; Dennis, E.A. High-Throughput Lipidomic Analysis of Fatty Acid Derived Eicosanoids and N-Acylethanolamines. *Biochim. Biophys. Acta Mol. Cell Biol. Lipids* **2011**, *1811*, 724–736. [CrossRef]
92. Miller, T.M.; Donnelly, M.K.; Crago, E.A.; Roman, D.M.; Sherwood, P.R.; Horowitz, M.B.; Poloyac, S.M. Rapid, Simultaneous Quantitation of Mono and Dioxygenated Metabolites of Arachidonic Acid in Human CSF and Rat Brain. *J. Chromatogr. B* **2009**, *877*, 3991–4000. [CrossRef]
93. Teav, T.; Gallart-Ayala, H.; van der Velpen, V.; Mehl, F.; Henry, H.; Ivanisevic, J. Merged Targeted Quantification and Untargeted Profiling for Comprehensive Assessment of Acylcarnitine and Amino Acid Metabolism. *Anal. Chem.* **2019**, *91*, 11757–11769. [CrossRef]
94. Wang, M.; Yang, R.; Mu, H.; Zeng, J.; Zhang, T.; Zhou, W.; Wang, S.; Tang, Y.; Li, H.; Zhang, C.; et al. A Simple and Precise Method for Measurement of Serum Free Carnitine and Acylcarnitines by Isotope Dilution HILIC-ESI-MS/MS. *Int. J. Mass Spectrom.* **2019**, *446*, 116208. [CrossRef]
95. Yang, Y.; Sadri, H.; Prehn, C.; Adamski, J.; Rehage, J.; Dänicke, S.; Saremi, B.; Sauerwein, H. Acylcarnitine Profiles in Serum and Muscle of Dairy Cows Receiving Conjugated Linoleic Acids or a Control Fat Supplement during Early Lactation. *J. Dairy Sci.* **2019**, *102*, 754–767. [CrossRef] [PubMed]

96. Ahmed, A.T.; MahmoudianDehkordi, S.; Bhattacharyya, S.; Arnold, M.; Liu, D.; Neavin, D.; Moseley, M.A.; Thompson, J.W.; Williams, L.S.J.; Louie, G.; et al. Acylcarnitine Metabolomic Profiles Inform Clinically-Defined Major Depressive Phenotypes. *J. Affect. Disord.* **2020**, *264*, 90–97. [CrossRef] [PubMed]
97. Chen, G.; Zhang, Q. Simultaneous Quantification of Free Fatty Acids and Acylcarnitines in Plasma Samples Using Dansylhydrazine Labeling and Liquid Chromatography–Triple Quadrupole Mass Spectrometry. *Anal. Bioanal. Chem.* **2020**. [CrossRef] [PubMed]
98. Kolar, M.J.; Nelson, A.T.; Chang, T.; Ertunc, M.E.; Christy, M.P.; Ohlsson, L.; Härröd, M.; Kahn, B.B.; Siegel, D.; Saghatelian, A. Faster Protocol for Endogenous Fatty Acid Esters of Hydroxy Fatty Acid (FAHFA) Measurements. *Anal. Chem.* **2018**, *90*, 5358–5365. [CrossRef]
99. Zhu, Q.-F.; Yan, J.-W.; Zhang, T.-Y.; Xiao, H.-M.; Feng, Y.-Q. Comprehensive Screening and Identification of Fatty Acid Esters of Hydroxy Fatty Acids in Plant Tissues by Chemical Isotope Labeling-Assisted Liquid Chromatography–Mass Spectrometry. *Anal. Chem.* **2018**, *90*, 10056–10063. [CrossRef]
100. Zhu, Q.-F.; Yan, J.-W.; Ni, J.; Feng, Y.-Q. FAHFA Footprint in the Visceral Fat of Mice across Their Lifespan. *Biochim. Biophys. Acta Mol. Cell Biol. Lipids* **2020**, *1865*, 158639. [CrossRef]
101. Hu, C.; Wang, M.; Duan, Q.; Han, X. Sensitive Analysis of Fatty Acid Esters of Hydroxy Fatty Acids in Biological Lipid Extracts by Shotgun Lipidomics after One-Step Derivatization. *Anal. Chim. Acta* **2020**, *1105*, 105–111. [CrossRef]
102. Tan, B.; William Yu, Y.; Francesca Monn, M.; Velocity Hughes, H.; O'Dell, D.K.; Michael Walker, J. Targeted Lipidomics Approach for Endogenous N-Acyl Amino Acids in Rat Brain Tissue. *J. Chromatogr. B* **2009**, *877*, 2890–2894. [CrossRef]
103. Zhu, M.; Xu, X.; Hou, Y.; Han, J.; Wang, J.; Zheng, Q.; Hao, H. Boronic Derivatization of Monoacylglycerol and Monitoring in Biofluids. *Anal. Chem.* **2019**, *91*, 6724–6729. [CrossRef]
104. Gao, F.; McDaniel, J.; Chen, Y.E.; Rockwell, H.; Lynes, D.M.; Tseng, Y.-H.; Sarangarajan, R.; Narain, R.N.; Kiebish, A.M. Monoacylglycerol Analysis Using MS/MSALL Quadruple Time of Flight Mass Spectrometry. *Metabolites* **2016**, *6*, 25. [CrossRef]
105. Ertl, V.M.; Höring, M.; Schött, H.-F.; Blücher, C.; Kjølbæk, L.; Astrup, A.; Burkhardt, R.; Liebisch, G. Quantification of Diacylglycerol and Triacylglycerol Species in Human Fecal Samples by Flow Injection Fourier Transform Mass Spectrometry. *Anal. Bioanal. Chem.* **2020**. [CrossRef]
106. Rashid, R.; Cazenave-Gassiot, A.; Gao, I.H.; Nair, Z.J.; Kumar, J.K.; Gao, L.; Kline, K.A.; Wenk, M.R. Comprehensive Analysis of Phospholipids and Glycolipids in the Opportunistic Pathogen Enterococcus Faecalis. *PLoS ONE* **2017**, *12*, e0175886. [CrossRef]
107. Harrison, K.A.; Bergman, B.C. *HPLC-MS/MS Methods for Diacylglycerol and Sphingolipid Molecular Species in Skeletal Muscle BT—High-Throughput Metabolomics: Methods and Protocols*; D'Alessandro, A., Ed.; Springer: New York, NY, USA, 2019; pp. 137–152. [CrossRef]
108. Bird, S.S.; Marur, V.R.; Sniatynski, M.J.; Greenberg, H.K.; Kristal, B.S. Serum Lipidomics Profiling Using LC–MS and High-Energy Collisional Dissociation Fragmentation: Focus on Triglyceride Detection and Characterization. *Anal. Chem.* **2011**, *83*, 6648–6657. [CrossRef]
109. Zeb, A. Triacylglycerols Composition, Oxidation and Oxidation Compounds in Camellia Oil Using Liquid Chromatography–Mass Spectrometry. *Chem. Phys. Lipids* **2012**, *165*, 608–614. [CrossRef]
110. Zheng, G.; Li, W. Profiling Membrane Glycerolipids during γ-Ray-Induced Membrane Injury. *BMC Plant Biol.* **2017**, *17*, 203. [CrossRef]
111. Wang, X.; Su, X.; Luo, Q.; Xu, J.; Chen, J.; Yan, X.; Chen, H. Profiles of Glycerolipids in Pyropia Haitanensis and Their Changes Responding to Agaro-Oligosaccharides. *J. Appl. Phycol.* **2014**, *26*, 2397–2404. [CrossRef]
112. Knific, T.; Vouk, K.; Smrkolj, Š.; Prehn, C.; Adamski, J.; Rižner, T.L. Models Including Plasma Levels of Sphingomyelins and Phosphatidylcholines as Diagnostic and Prognostic Biomarkers of Endometrial Cancer. *J. Steroid Biochem. Mol. Biol.* **2018**, *178*, 312–321. [CrossRef]
113. Yan, Y.; Du, Z.; Chen, C.; Li, J.; Xiong, X.; Zhang, Y.; Jiang, H. Lysophospholipid Profiles of Apolipoprotein E-Deficient Mice Reveal Potential Lipid Biomarkers Associated with Atherosclerosis Progression Using Validated UPLC-QTRAP-MS/MS-Based Lipidomics Approach. *J. Pharm. Biomed. Anal.* **2019**, *171*, 148–157. [CrossRef]
114. Uhl, O.; Glaser, C.; Demmelmair, H.; Koletzko, B. Reversed Phase LC/MS/MS Method for Targeted Quantification of Glycerophospholipid Molecular Species in Plasma. *J. Chromatogr. B* **2011**, *879*, 3556–3564. [CrossRef]

115. Wang, X.; Xu, Y.; Song, X.; Jia, Q.; Zhang, X.; Qian, Y.; Qiu, J. Analysis of Glycerophospholipid Metabolism after Exposure to PCB153 in PC12 Cells through Targeted Lipidomics by UHPLC-MS/MS. *Ecotoxicol. Environ. Saf.* **2019**, *169*, 120–127. [CrossRef] [PubMed]
116. Deeley, J.M.; Thomas, M.C.; Truscott, R.J.W.; Mitchell, T.W.; Blanksby, S.J. Identification of Abundant Alkyl Ether Glycerophospholipids in the Human Lens by Tandem Mass Spectrometry Techniques. *Anal. Chem.* **2009**, *81*, 1920–1930. [CrossRef] [PubMed]
117. She, Y.; Song, J.; Yang, E.; Zhao, L.; Zhong, Y.; Rui, W.; Feng, Y.; Wu, X. Rapid Identification of Glycerophospholipids from RAW264.7 Cells by UPLC/ESI -QTOF-MS. *Biomed. Chromatogr.* **2014**, *28*, 1744–1755. [CrossRef]
118. She, Y.; Zheng, Q.; Xiao, X.; Wu, X.; Feng, Y. An Analysis on the Suppression of NO and PGE2 by Diphenylheptane A and Its Effect on Glycerophospholipids of Lipopolysaccharide-Induced RAW264.7 Cells with UPLC/ESI-QTOF-MS. *Anal. Bioanal. Chem.* **2016**, *408*, 3185–3201. [CrossRef]
119. Sun, T.; Pawlowski, S.; Johnson, M.E. Highly Efficient Microscale Purification of Glycerophospholipids by Microfluidic Cell Lysis and Lipid Extraction for Lipidomics Profiling. *Anal. Chem.* **2011**, *83*, 6628–6634. [CrossRef]
120. Maciel, E.; Neves, B.M.; Santinha, D.; Reis, A.; Domingues, P.; Teresa Cruz, M.; Pitt, A.R.; Spickett, C.M.; Domingues, M.R.M. Detection of Phosphatidylserine with a Modified Polar Head Group in Human Keratinocytes Exposed to the Radical Generator AAPH. *Arch. Biochem. Biophys.* **2014**, *548*, 38–45. [CrossRef]
121. Stübiger, G.; Aldover-Macasaet, E.; Bicker, W.; Sobal, G.; Willfort-Ehringer, A.; Pock, K.; Bochkov, V.; Widhalm, K.; Belgacem, O. Targeted Profiling of Atherogenic Phospholipids in Human Plasma and Lipoproteins of Hyperlipidemic Patients Using MALDI-QIT-TOF-MS/MS. *Atherosclerosis* **2012**, *224*, 177–186. [CrossRef]
122. Basit, A.; Piomelli, D.; Armirotti, A. Rapid Evaluation of 25 Key Sphingolipids and Phosphosphingolipids in Human Plasma by LC-MS/MS. *Anal. Bioanal. Chem.* **2015**, *407*, 5189–5198. [CrossRef]
123. Mi, S.; Zhao, Y.-Y.; Dielschneider, R.F.; Gibson, S.B.; Curtis, J.M. An LC/MS/MS Method for the Simultaneous Determination of Individual Sphingolipid Species in B Cells. *J. Chromatogr. B* **2016**, *1031*, 50–60. [CrossRef]
124. Chipeaux, C.; de Person, M.; Burguet, N.; Billette de Villemeur, T.; Rose, C.; Belmatoug, N.; Héron, S.; Le Van Kim, C.; Franco, M.; Moussa, F. Optimization of Ultra-High Pressure Liquid Chromatography–Tandem Mass Spectrometry Determination in Plasma and Red Blood Cells of Four Sphingolipids and Their Evaluation as Biomarker Candidates of Gaucher's Disease. *J. Chromatogr. A* **2017**, *1525*, 116–125. [CrossRef]
125. Li, J.; Hu, C.; Zhao, X.; Dai, W.; Chen, S.; Lu, X.; Xu, G. Large-Scaled Human Serum Sphingolipid Profiling by Using Reversed-Phase Liquid Chromatography Coupled with Dynamic Multiple Reaction Monitoring of Mass Spectrometry: Method Development and Application in Hepatocellular Carcinoma. *J. Chromatogr. A* **2013**, *1320*, 103–110. [CrossRef]
126. Sullards, M.C.; Liu, Y.; Chen, Y.; Merrill, A.H. Analysis of Mammalian Sphingolipids by Liquid Chromatography Tandem Mass Spectrometry (LC-MS/MS) and Tissue Imaging Mass Spectrometry (TIMS). *Biochim. Biophys. Acta Mol. Cell Biol. Lipids* **2011**, *1811*, 838–853. [CrossRef]
127. Bui, H.H.; Leohr, J.K.; Kuo, M.-S. Analysis of Sphingolipids in Extracted Human Plasma Using Liquid Chromatography Electrospray Ionization Tandem Mass Spectrometry. *Anal. Biochem.* **2012**, *423*, 187–194. [CrossRef]
128. Scherer, M.; Böttcher, A.; Schmitz, G.; Liebisch, G. Sphingolipid Profiling of Human Plasma and FPLC-Separated Lipoprotein Fractions by Hydrophilic Interaction Chromatography Tandem Mass Spectrometry. *Biochim. Biophys. Acta Mol. Cell Biol. Lipids* **2011**, *1811*, 68–75. [CrossRef]
129. T'Kindt, R.; Jorge, L.; Dumont, E.; Couturon, P.; David, F.; Sandra, P.; Sandra, K. Profiling and Characterizing Skin Ceramides Using Reversed-Phase Liquid Chromatography–Quadrupole Time-of-Flight Mass Spectrometry. *Anal. Chem.* **2012**, *84*, 403–411. [CrossRef]
130. Liao, H.W.; Lin, S.W.; Lin, Y.T.; Lee, C.H.; Kuo, C.H. Identification of Potential Sphingomyelin Markers for the Estimation of Hematocrit in Dried Blood Spots via a Lipidomic Strategy. *Anal. Chim. Acta* **2018**, *1003*, 34–41. [CrossRef]
131. Huang, Q.; Liu, D.; Xin, B.; Cechner, K.; Zhou, X.; Wang, H.; Zhou, A. Quantification of Monosialogangliosides in Human Plasma through Chemical Derivatization for Signal Enhancement in LC–ESI-MS. *Anal. Chim. Acta* **2016**, *929*, 31–38. [CrossRef] [PubMed]

132. Hájek, R.; Jirásko, R.; Lísa, M.; Cífková, E.; Holčapek, M. Hydrophilic Interaction Liquid Chromatography–Mass Spectrometry Characterization of Gangliosides in Biological Samples. *Anal. Chem.* **2017**, *89*, 12425–12432. [CrossRef] [PubMed]
133. Broughton, R.; Ruíz-Lopez, N.; Hassall, K.L.; Martínez-Force, E.; Garcés, R.; Salas, J.J.; Beaudoin, F. New Insights in the Composition of Wax and Sterol Esters in Common and Mutant Sunflower Oils Revealed by ESI-MS/MS. *Food Chem.* **2018**, *269*, 70–79. [CrossRef]
134. Reinicke, M.; Schröter, J.; Müller-Klieser, D.; Helmschrodt, C.; Ceglarek, U. Free Oxysterols and Bile Acids Including Conjugates—Simultaneous Quantification in Human Plasma and Cerebrospinal Fluid by Liquid Chromatography-Tandem Mass Spectrometry. *Anal. Chim. Acta* **2018**, *1037*, 245–255. [CrossRef] [PubMed]
135. Piqueras, M.; Theotoka, D.; Sarohia, G.S.; Bhattacharya, S.K. *Analyses of Cholesterol and Derivatives in Ocular Tissues Using LC-MS/MS Methods BT—Metabolomics: Methods and Protocols*; Bhattacharya, S.K., Ed.; Springer: New York, NY, USA, 2019; pp. 53–59. [CrossRef]
136. Kunz, S.; Matysik, S. A Comprehensive Method to Determine Sterol Species in Human Faeces by GC-Triple Quadrupole MS. *J. Steroid Biochem. Mol. Biol.* **2019**, *190*, 99–103. [CrossRef]
137. Schött, H.-F.; Krautbauer, S.; Höring, M.; Liebisch, G.; Matysik, S. A Validated, Fast Method for Quantification of Sterols and Gut Microbiome Derived 5α/β-Stanols in Human Feces by Isotope Dilution LC–High-Resolution MS. *Anal. Chem.* **2018**, *90*, 8487–8494. [CrossRef]
138. Ceglarek, U.; Dittrich, J.; Leopold, J.; Helmschrodt, C.; Becker, S.; Staab, H.; Richter, O.; Rohm, S.; Aust, G. Free Cholesterol, Cholesterol Precursor and Plant Sterol Levels in Atherosclerotic Plaques Are Independently Associated with Symptomatic Advanced Carotid Artery Stenosis. *Atherosclerosis* **2020**, *295*, 18–24. [CrossRef] [PubMed]
139. Takeshima, M.; Ogihara, H.M.; Kataoka, H. Sterol Characteristics in Silkworm Brain and Various Tissues Characterized by Precise Sterol Profiling Using LC-MS/MS. *Int. J. Mol. Sci.* **2019**, *20*, 4840. [CrossRef] [PubMed]
140. Matysik, S.; Liebisch, G. Quantification of Steroid Hormones in Human Serum by Liquid Chromatography-High Resolution Tandem Mass Spectrometry. *J. Chromatogr. A* **2017**, *1526*, 112–118. [CrossRef] [PubMed]
141. Moon, J.-Y.; Lee, H.S.; Kim, J.H.; Lee, J.H.; Choi, M.H. Supported Liquid Extraction Coupled to Gas Chromatography-Selective Mass Spectrometric Scan Modes for Serum Steroid Profiling. *Anal. Chim. Acta* **2018**, *1037*, 281–292. [CrossRef]
142. Drotleff, B.; Hallschmid, M.; Lämmerhofer, M. Quantification of Steroid Hormones in Plasma Using a Surrogate Calibrant Approach and UHPLC-ESI-QTOF-MS/MS with SWATH-Acquisition Combined with Untargeted Profiling. *Anal. Chim. Acta* **2018**, *1022*, 70–80. [CrossRef]
143. Hu, T.; An, Z.; Shi, C.; Li, P.; Liu, L. A Sensitive and Efficient Method for Simultaneous Profiling of Bile Acids and Fatty Acids by UPLC-MS/MS. *J. Pharm. Biomed. Anal.* **2020**, *178*, 112815. [CrossRef] [PubMed]
144. LeníLek, M.; Vecka, M.; Žížalová, K.; Vítek, L. Comparison of Simple Extraction Procedures in Liquid Chromatography mass Spectrometry Based Determination of Serum 7α-Hydroxy-4-Cholesten-3-One, a Surrogate Marker of Bile Acid Synthesis. *J. Chromatogr. B* **2016**, *1033–1034*, 317–320. [CrossRef]
145. Ulaszewska, M.M.; Mancini, A.; Garcia-Aloy, M.; Del Bubba, M.; Tuohy, K.M.; Vrhovsek, U. Isotopic Dilution Method for Bile Acid Profiling Reveals New Sulfate Glycine-Conjugated Dihydroxy Bile Acids and Glucuronide Bile Acids in Serum. *J. Pharm. Biomed. Anal.* **2019**, *173*, 1–17. [CrossRef]
146. Franco, P.; Porru, E.; Fiori, J.; Gioiello, A.; Cerra, B.; Roda, G.; Caliceti, C.; Simoni, P.; Roda, A. Identification and Quantification of Oxo-Bile Acids in Human Faeces with Liquid Chromatography–Mass Spectrometry: A Potent Tool for Human Gut Acidic Sterolbiome Studies. *J. Chromatogr. A* **2019**, *1585*, 70–81. [CrossRef]
147. Higashi, T.; Watanabe, S.; Tomaru, K.; Yamazaki, W.; Yoshizawa, K.; Ogawa, S.; Nagao, H.; Minato, K.; Maekawa, M.; Mano, N. Unconjugated Bile Acids in Rat Brain: Analytical Method Based on LC/ESI-MS/MS with Chemical Derivatization and Estimation of Their Origin by Comparison to Serum Levels. *Steroids* **2017**, *125*, 107–113. [CrossRef]
148. Stinco, C.M.; Benítez-González, A.M.; Meléndez-Martínez, A.J.; Hernanz, D.; Vicario, I.M. Simultaneous Determination of Dietary Isoprenoids (Carotenoids, Chlorophylls and Tocopherols) in Human Faeces by Rapid Resolution Liquid Chromatography. *J. Chromatogr. A* **2019**, *1583*, 63–72. [CrossRef]

149. Zhang, X.; Guo, T.; Xiang, T.; Dong, Y.; Zhang, J.; Zhang, L. Quantitation of Isoprenoids for Natural Rubber Biosynthesis in Natural Rubber Latex by Liquid Chromatography with Tandem Mass Spectrometry. *J. Chromatogr. A* **2018**, *1558*, 115–119. [CrossRef]
150. Baidoo, E.E.K.; Wang, G.; Joshua, C.J.; Benites, V.T.; Keasling, J.D. *Liquid Chromatography and Mass Spectrometry Analysis of Isoprenoid Intermediates in Escherichia Coli BT—Microbial Metabolomics: Methods and Protocols*; Baidoo, E.E.K., Ed.; Springer: New York, NY, USA, 2019; pp. 209–224. [CrossRef]
151. Chhonker, Y.S.; Haney, S.L.; Bala, V.; Holstein, S.A.; Murry, D.J. Simultaneous Quantitation of Isoprenoid Pyrophosphates in Plasma and Cancer Cells Using LC-MS/MS. *Molecules* **2018**, *23*, 3275. [CrossRef]
152. Lim, D.; Ikeda, A.; Vu, K.K.-T.; Yamaguchi, K.T.; Tyner, T.R.; Hasson, A.S. Method Development for the Measurement of Quinone Levels in Urine. *J. Chromatogr. B* **2011**, *879*, 3592–3598. [CrossRef]
153. Kaiser, P.; Geyer, R.; Surmann, P.; Fuhrmann, H. LC–MS Method for Screening Unknown Microbial Carotenoids and Isoprenoid Quinones. *J. Microbiol. Methods* **2012**, *88*, 28–34. [CrossRef]
154. Lukasiewicz, J.; Jachymek, W.; Niedziela, T.; Kenne, L.; Lugowski, C. Structural Analysis of the Lipid A Isolated from Hafnia Alvei 32 and PCM 1192 Lipopolysaccharides. *J. Lipid Res.* **2010**, *51*, 564–574. [CrossRef]
155. Sándor, V.; Dörnyei, Á.; Makszin, L.; Kilár, F.; Péterfi, Z.; Kocsis, B.; Kilár, A. Characterization of Complex, Heterogeneous Lipid A Samples Using HPLC–MS/MS Technique I. Overall Analysis with Respect to Acylation, Phosphorylation and Isobaric Distribution. *J. Mass Spectrom.* **2016**, *51*, 1043–1063. [CrossRef]
156. Sawyer, W.S.; Wang, L.; Uehara, T.; Tamrakar, P.; Prathapam, R.; Mostafavi, M.; Metzger IV, L.E.; Feng, B.; Baxter Rath, C.M. Targeted Lipopolysaccharide Biosynthetic Intermediate Analysis with Normal-Phase Liquid Chromatography Mass Spectrometry. *PLoS ONE* **2019**, *14*, e0211803. [CrossRef]
157. Paulus, C.; Rebets, Y.; Zapp, J.; Rückert, C.; Kalinowski, J.; Luzhetskyy, A. New Alpiniamides From Streptomyces Sp. IB2014/011-12 Assembled by an Unusual Hybrid Non-Ribosomal Peptide Synthetase Trans-AT Polyketide Synthase Enzyme. *Front. Microbiol.* **2018**, *9*, 1959. [CrossRef] [PubMed]
158. Sun, F.; Xu, S.; Jiang, F.; Liu, W. Genomic-Driven Discovery of an Amidinohydrolase Involved in the Biosynthesis of Mediomycin A. *Appl. Microbiol. Biotechnol.* **2018**, *102*, 2225–2234. [CrossRef] [PubMed]
159. Bhan, N.; Cress, B.F.; Linhardt, R.J.; Koffas, M. Expanding the Chemical Space of Polyketides through Structure-Guided Mutagenesis of Vitis Vinifera Stilbene Synthase. *Biochimie* **2015**, *115*, 136–143. [CrossRef] [PubMed]
160. Rocchetti, G.; Lucini, L.; Giuberti, G.; Bhumireddy, S.R.; Mandal, R.; Trevisan, M.; Wishart, D.S. Transformation of Polyphenols Found in Pigmented Gluten-Free Flours during in Vitro Large Intestinal Fermentation. *Food Chem.* **2019**, *298*, 125068. [CrossRef] [PubMed]
161. Wen, Q.; Li, H.-L.; Mai, S.-Y.; Tan, Y.-F.; Chen, F. Tissue Distribution of Active Principles from Alpiniae Oxyphyllae Fructus Extract: An Experimental Study in Rats. *Curr. Pharm. Anal.* **2019**, 286–293. [CrossRef]
162. Chen, F.; Li, H.-L.; Tan, Y.-F.; Li, Y.-H.; Lai, W.-Y.; Guan, W.-W.; Zhang, J.-Q.; Zhao, Y.-S.; Qin, Z.-M. Identification of Known Chemicals and Their Metabolites from Alpinia Oxyphylla Fruit Extract in Rat Plasma Using Liquid Chromatography/Tandem Mass Spectrometry (LC–MS/MS) with Selected Reaction Monitoring. *J. Pharm. Biomed. Anal.* **2014**, *97*, 166–177. [CrossRef]
163. Manning, S.R.; La Claire II, J.W. Isolation of Polyketides from Prymnesium Parvum (Haptophyta) and Their Detection by Liquid Chromatography/Mass Spectrometry Metabolic Fingerprint Analysis. *Anal. Biochem.* **2013**, *442*, 189–195. [CrossRef]
164. Rodríguez-López, C.E.; Hernández-Brenes, C.; Treviño, V.; Díaz de la Garza, R.I. Avocado Fruit Maturation and Ripening: Dynamics of Aliphatic Acetogenins and Lipidomic Profiles from Mesocarp, Idioblasts and Seed. *BMC Plant Biol.* **2017**, *17*, 159. [CrossRef]
165. Lísa, M.; Holčapek, M. High-Throughput and Comprehensive Lipidomic Analysis Using Ultrahigh-Performance Supercritical Fluid Chromatography–Mass Spectrometry. *Anal. Chem.* **2015**, *87*, 7187–7195. [CrossRef]
166. Wood, P.L.; Scoggin, K.; Ball, B.A.; Troedsson, M.H.; Squires, E.L. Lipidomics of Equine Sperm and Seminal Plasma: Identification of Amphiphilic (O-Acyl)-ω-Hydroxy-Fatty Acids. *Theriogenology* **2016**, *86*, 1212–1221. [CrossRef]
167. Montefusco, D.J.; Allegood, J.C.; Spiegel, S.; Cowart, L.A. Non-Alcoholic Fatty Liver Disease: Insights from Sphingolipidomics. *Biochem. Biophys. Res. Commun.* **2018**, *504*, 608–616. [CrossRef]

168. Yang, Y.; Lee, M.; Fairn, G.D. Phospholipid Subcellular Localization and Dynamics. *J. Biol. Chem.* **2018**, *293*, 6230–6240. [CrossRef]
169. López-Bascón, M.A.; Calderón-Santiago, M.; Sánchez-Ceinos, J.; Fernández-Vega, A.; Guzmán-Ruiz, R.; López-Miranda, J.; Malagon, M.M.; Priego-Capote, F. Influence of Sample Preparation on Lipidomics Analysis of Polar Lipids in Adipose Tissue. *Talanta* **2018**, *177*, 86–93. [CrossRef]
170. Bollinger, J.G.; Ii, H.; Sadilek, M.; Gelb, M.H. Improved Method for the Quantification of Lysophospholipids Including Enol Ether Species by Liquid Chromatography-Tandem Mass Spectrometry. *J. Lipid Res.* **2010**, *51*, 440–447. [CrossRef]
171. Ahmad, S.; Kalra, H.; Gupta, A.; Raut, B.; Hussain, A.; Rahman, M.A. HybridSPE: A Novel Technique to Reduce Phospholipid-Based Matrix Effect in LC-ESI-MS Bioanalysis. *J. Pharm. Bioallied Sci.* **2012**, *4*, 267–275. [CrossRef]
172. Criado-Navarro, I.; Mena-Bravo, A.; Calderón-Santiago, M.; Priego-Capote, F. Determination of Glycerophospholipids in Vegetable Edible Oils: Proof of Concept to Discriminate Olive Oil Categories. *Food Chem.* **2019**, *299*, 125136. [CrossRef]
173. Helmer, P.O.; Korf, A.; Hayen, H. Analysis of Artificially Oxidized Cardiolipins and Monolyso-Cardiolipins via Liquid Chromatography/High-Resolution Mass Spectrometry and Kendrick Mass Defect Plots after Hydrophilic Interaction Liquid Chromatography Based Sample Preparation. *Rapid Commun. Mass Spectrom.* **2020**, *34*, e8566. [CrossRef]
174. John, C.; Werner, P.; Worthmann, A.; Wegner, K.; Tödter, K.; Scheja, L.; Rohn, S.; Heeren, J.; Fischer, M. A Liquid Chromatography-Tandem Mass Spectrometry-Based Method for the Simultaneous Determination of Hydroxy Sterols and Bile Acids. *J. Chromatogr. A* **2014**, *1371*, 184–195. [CrossRef]
175. Ms, U.; Ferdosh, S.; Haque Akanda, M.J.; Ghafoor, K.; Rukshana, A.H.; Ali, M.E.; Kamaruzzaman, B.Y.; Fauzi, M.B.; Sharifudin Shaarani, H.S.; Islam Sarker, M.Z. Techniques for the Extraction of Phytosterols and Their Benefits in Human Health: A Review. *Sep. Sci. Technol.* **2018**, *53*, 2206–2223. [CrossRef]
176. McDonald, J.G.; Thompson, B.M.; McCrum, E.C.; Russell, D.W. Extraction and Analysis of Sterols in Biological Matrices by High Performance Liquid Chromatography Electrospray Ionization Mass Spectrometry. *Methods Enzymol.* **2007**, *432*, 145–170. [CrossRef]
177. Liakh, I.; Pakiet, A.; Sledzinski, T.; Mika, A. Modern Methods of Sample Preparation for the Analysis of Oxylipins in Biological Samples. *Molecules* **2019**, *24*, 1639. [CrossRef] [PubMed]
178. Kodama, H. *GC-MS Methods for Tobacco Constituents BT—Gas Chromatography/Mass Spectrometry*; Linskens, H.F., Jackson, J.F., Eds.; Springer: Berlin/Heidelberg, Germany, 1986; pp. 277–298. [CrossRef]
179. Meléndez-Martínez, A.J.; Stinco, C.M.; Brahm, P.M.; Vicario, I.M. *Analysis of Carotenoids and Tocopherols in Plant Matrices and Assessment of Their In Vitro Antioxidant Capacity BT—Plant Isoprenoids: Methods and Protocols*; Rodríguez-Concepción, M., Ed.; Springer: New York, NY, USA, 2014; pp. 77–97. [CrossRef]
180. Yamada, T.; Bamba, T. *Lipid Profiling by Supercritical Fluid Chromatography/Mass Spectrometry BT—Lipidomics*; Wood, P., Ed.; Springer: New York, NY, USA, 2017; pp. 109–131. [CrossRef]
181. Britton, G.; Young, A.J. *Methods for the Isolation and Analysis of Carotenoids BT—Carotenoids in Photosynthesis*; Young, A.J., Britton, G., Eds.; Springer: Dordrecht, The Netherlands, 1993; pp. 409–457. [CrossRef]
182. Hadj-Mahammed, M.; Badjah-Hadj-Ahmed, Y.; Meklati, B.Y. Behaviour of Polymethoxylated and Polyhydroxylated Flavones by Carbon Dioxide Supercritical Fluid Chromatography with Flame Ionization and Fourier Transform Infrared Detectors. *Phytochem. Anal.* **1993**, *4*, 275–278. [CrossRef]
183. Lebeau, J.; Venkatachalam, M.; Fouillaud, M.; Petit, T.; Vinale, F.; Dufossé, L.; Caro, Y. Production and New Extraction Method of Polyketide Red Pigments Produced by Ascomycetous Fungi from Terrestrial and Marine Habitats. *J. Fungi (Basel Switz.)* **2017**, *3*, 34. [CrossRef]

184. Nieman, D.C.; Kay, C.D.; Rathore, A.S.; Grace, M.H.; Strauch, R.C.; Stephan, E.H.; Sakaguchi, C.A.; Lila, M.A. Increased Plasma Levels of Gut-Derived Phenolics Linked to Walking and Running Following Two Weeks of Flavonoid Supplementation. *Nutrients* **2018**, *10*, 1718. [CrossRef]
185. Nguyen, M.P.; Tran, L.V.H.; Namgoong, H.; Kim, Y.-H. Applications of Different Solvents and Conditions for Differential Extraction of Lipopolysaccharide in Gram-Negative Bacteria. *J. Microbiol.* **2019**, *57*, 644–654. [CrossRef]