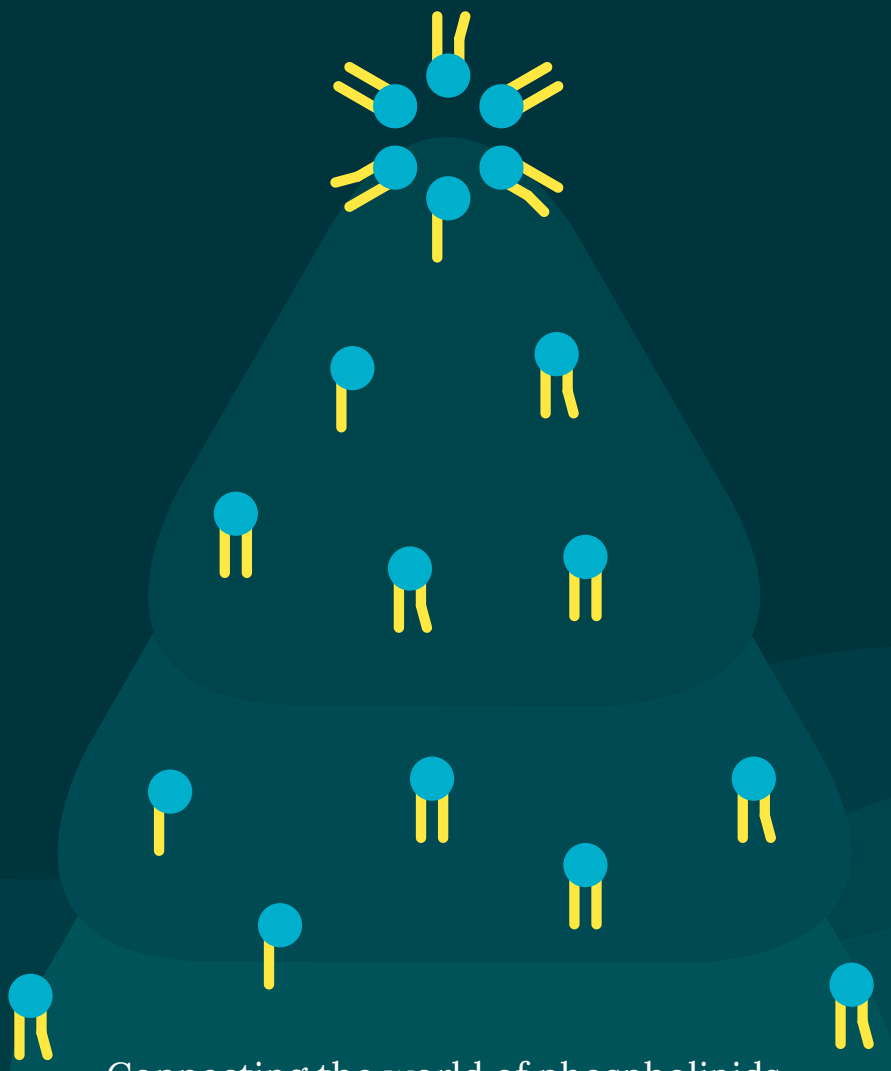
Phospholipid Research Center

Phospholipid Insights

NEWSLETTER | VOLUME 12, NO. 1 | DECEMBER 2018



Connecting the world of phospholipids.

www.phospholipid-institute.com

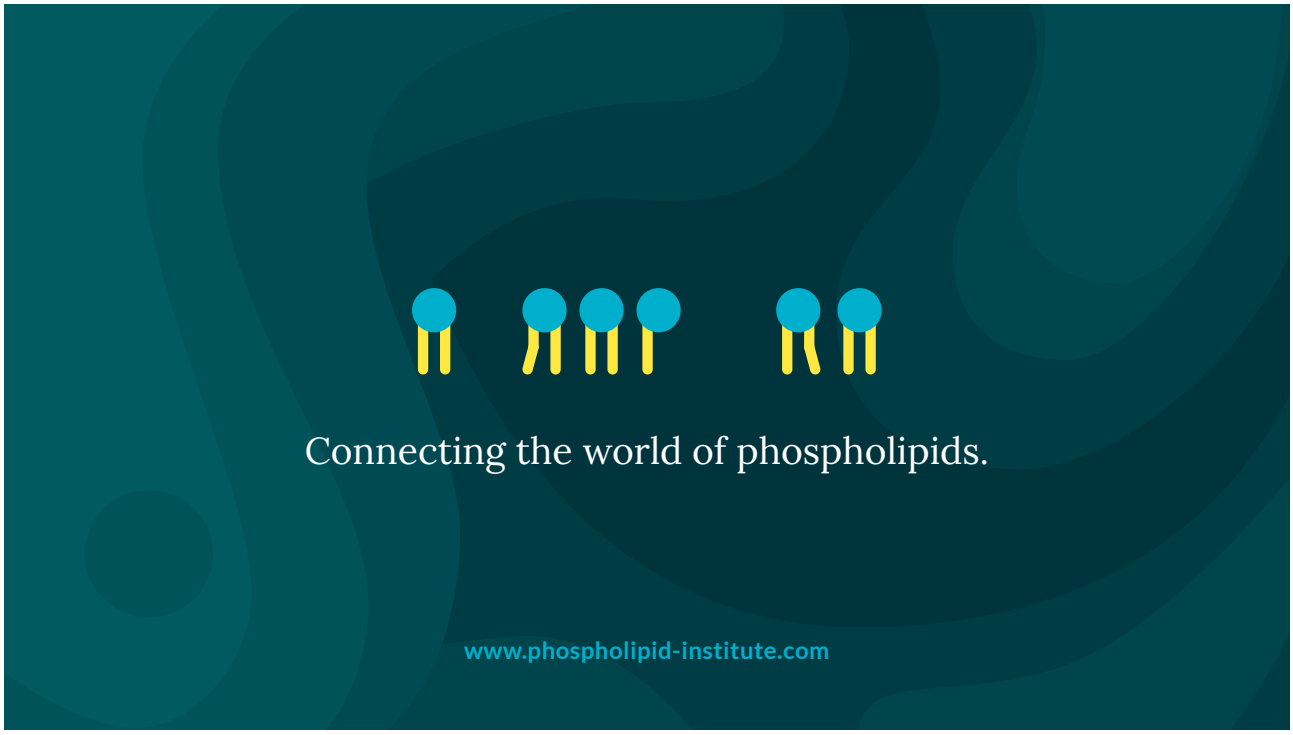


Table of contents

"Connecting the World of Phospholipids" – Old Mission with a New Look

As most of you already noticed our homepage has a new look. Our previous mission connecting the world of phospholipid research is now clearly visible on our homepage. To live this slogan we organized and supported several meetings in the last years. On June June 25th–26th, 2018, we invited all our funded research groups to a scientific meeting – called "Researchers Day". In total 65 participants enjoyed in-depth discussions and presentations of research projects in a familiar ambiance. This event was meant to encourage networking among the researchers. It was well received and will be repeated in 2020. Furthermore, in 2018 the Phospholipid Research Center became more internationally known, since about 50 % of the supported projects are coming from outside Germany.

In this issue, we are pleased to present the scientific work of Dr. Jyrki Viidanoja as a special article devoted to lipid related analytical methods. Dr. Jyrki Viidanoja is a specialist in LC/MS analytics and works as a Research & Development Engineer for Thermo Fisher Scientific in Finland (previous Technology Centre, Kilpilahti, Neste Corporation). In the present research article he describes the development of a LC–ESI-MS/MS method for simultaneous (semi)-quantification of a very large array of Phospholipid (PL) classes in bio-oils and fats. This method is a great inspiration and can be transferred to other disciplines. We thank Dr. Jyrki Viidanoja for his valuable contribution.

In 2019, we intend to become even more active compared to 2018. First, we will again organize our biannual International Symposium on Phospholipids in Pharmaceutical Research in Heidelberg on September 9th–10th, 2019. Second, we plan to organize a workshop on the CRS Symposium in Valencia, Spain and to explore and stimulate cooperation's with other organizations promoting the use of phospholipids in liposomes.

Finally, at the end of this year 2018, we would like to thank all members for their valuable contributions and wish all of you a Successful 2019!

Peter van Hoogevest
Managing Director
Phospholipid Research Center

News from the Phospholipid Research Center

General Meeting of the Phospholipid Research Center e. V.

The General Meeting of the Phospholipid Research Center e. V. (PRC) took place on June 25th, 2018 (Hotel Residenz Limburgerhof, Limburgerhof) immediately after the Researchers Day 2018. 21 members with voting rights and two guests joined the meeting.

Each member of the Phospholipid Research Center e. V. is very welcome to join future general meetings and to stimulate our organization with new ideas.

Organization and Management Board

Prof. A. Blume	President
Prof. C. Müller-Goymann	Vice President
PD Dr. P. van Hoogevest	Managing Director
Dr. D. Gutekunst	Deputy Managing Director
B. Merz	Management Assistant

Facts and numbers of the PRC:

Meeting of the Scientific Advisory Council

On January 29th and June 26th the Scientific Advisory Council (Prof. Th. Andresen, Prof. A. Blume, Prof. G. Fricker, Dr. F. Martin, Prof. C. Müller-Goymann, Prof. G. Storm and Dr. R.-O. Quinkert) met, together with the management, for discussing new findings and reports of ongoing projects as well as for evaluating new research proposals.

At the first meeting of 2018, Prof. A. Blume welcomed a new member of the Scientific Advisory Council, Prof. Th. L. Andresen from DTU Lyngby/ Copenhagen, Denmark. Prof. Th. L. Andresen is an expert in drug delivery and nanomedicine with a special focus on the use of liposomal systems in cancer therapy. We are pleased to welcome Prof. Andresen as a valuable member of the advisory board.

Due to the increasing number of funded research projects, the advisory council decided to adapt the formal requirements for the research proposals and interim reports. In order to enable an in-depth discussion of each project it is necessary that the documents fit the general requirements. A mismatch will automatically result in rejection. Corresponding sample forms and more details can be found on the PRC homepage:

www.phospholipide-institute.com.

New funded Projects

In 2018 the PRC decided to support the following research projects. With these seven projects, the total number of ongoing funded projects increased up to 32.

Development of phospholipid-based antimalarial tablets of azadirachta indica leaf extract and artemether/lumefantrine for oral delivery.
Prof. A. A. Attama
University of Nigeria/Africa

Phospholipids as metastases-targeting molecules using barcoding as a new research tool in liposome discovery.
Prof. A. Schroeder
Technion Research & Development Foundation Ltd., Israel

Development and analysis of different phospholipid formulations for dermal application and their effect on human dermal cell viability.
Prof. C. Valenta
University of Vienna/Austria

Bottom-up designed synthetic bacteria – a tool to develop new antibiotic strategies.
Prof. T. Gutsmann
Forschungszentrum Borstel/Germany

Research on the loading of exosomes.
Prof. J.-C. Leroux
ETH Zurich/Switzerland

Theoretical model to describe formation and stability of liposome-drug complexes.
Prof. S. May
North Dakota State University/USA

Liposome – Extracellular Vesicle Hybrids for Therapeutic RNA Delivery.
Prof. R. M. Schiffelers
University Medical Center Utrecht/The Netherlands

Publications

Following publications, related to projects supported by the Phospholipid Research Center were made during 2018:

Mixing behaviour of asymmetrical glycerol diether bolalipids with saturated and unsaturated phosphatidylcholines.
Mueller S., Meister A., Otto C., Hause G., Drescher S.
Biophys Chem. 2018; 238:39-48.

Investigations of the influence of liposome composition on vesicle stability and drug transfer in human plasma: a transfer study.
Holzschuh S., Kaeß K., Bossa G.V., Decker C., Fahr A., May S.
J Liposome Res. 2018; 28(1):22–34.

Study on the in situ aggregation of liposomes with negatively charged phospholipids for use as injectable depot formulation.
Rahnfeld L., Thamm J., Steiniger F., van Hoogevest P., Luciani P.
Colloids Surf B Biointerfaces. 2018; 168:10-17.

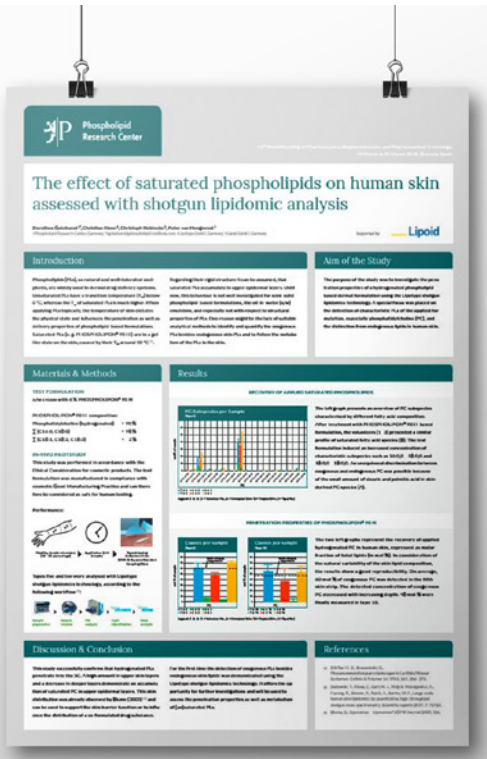
Physicochemical characterization of natural phospholipid excipients with varying PC content.
Otto F., Brezesinski G., van Hoogevest P., Neubert R.H.H.
Colloids Surf A. 2018; 558:291–296.

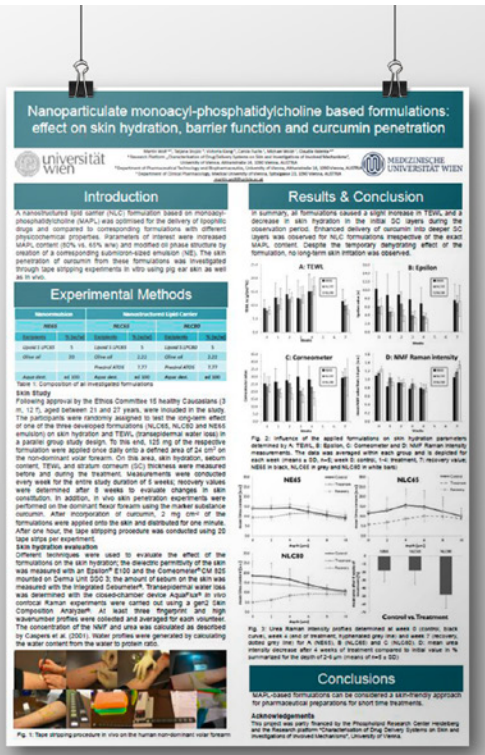
Mixing behaviour of bilayer-forming phosphatidylcholines with single-chain alkyl-branched bolalipids: Effect of lateral chain length.
Mueller S., Kind M., Gruhle K., Hause G., Meister A., Drescher S.
Biophys Chem. 2019; 244:1–10.

NLC versus nanoemulsions: Effect on physiological skin parameters during regular in vivo application and impact on drug penetration.
Wolf M., Klang V., Stojcic T., Fuchs C., Wolzt M., Valenta C.
Int J Pharm. 2018; 549:343–351.

Monoacyl-phospatidylcholine based drug delivery systems for lipophilic drugs: Nanostructured lipid carriers vs. nano-sized emulsions.
Wolf M., Reiter F., Heuser T., Kotisch H., Klang V., Valenta C.
J Drug Del Sci Technol. 2018; 46:490-497.

Poster Presentations 2018





The effect of saturated phospholipids on human skin assessed with shotgun lipidomic analysis (left Poster)
Gutekunst D., Klose C., Heidecke C., van Hoogevest P.
11th World Meeting on Pharmaceutics, Biopharmaceutics and Pharmaceutical Technology, Spain

Nanoparticulate monoacyl-phosphatidylcholine based formulations: Effect on skin hydration, barrier function and curcumin penetration (right Poster)
Wolf M., Stojcic T., Klang V., Fuchs C., Wolzt M., Valenta C.
Skin Forum, Estonia

Miscibility study of phospholipids with oils and fats for the liquid-filling of hard capsules
Grüne L., Bunjes H.
Annual Meeting of the German Pharmaceutical Society – DPhG Pharmaceutical Science: Structure, Function and Application, Germany

Chemical and acoustic characterization of a novel ultrasound contrast agent
Langeveld S.A.G., Beekers I., van der Stehen A.F.W., de Jong N., Kooiman K.
IEEE International Ultrasonics Symposium, Japan

Phosphatidylserine enriched phospholipids as anti-inflammatory agents
Klein M., Mauch S., Ramos G., Hofmann U., Meister A., Mäder K.
Controlled Release Society

Polyion-induced liposomal aggregates for antitubercular drug delivery
Sciolla F., Truzzolillo D., Rinaldi F., Hanieh P.N., Carafa M., Bordi F., Sennato S.
Nanomedicine Rome, Italy

Congress Reports

Researcher's Day 2018

Phospholipid Research Center, June 25th, 2018
In summer 2018, the Phospholipid Research Center invited all principle investigators and their PhD students or Post-docs in charge of funded projects to a big meet and greet. This so-called Researcher's Day focused on talented young scientist, to give them the chance presenting and discussing their research topics and results in presence of experts. The purpose of the meeting was to bring the researchers together and offer a platform for networking and exchange of scientific ideas. The sixty participants were categorized in three discussion groups related to parenteral, oral and topical administration of phospholipids, respectively. Small, specialized groups should allow for in-depth discussions among scientist having the same main interests. Members of the Scientific Advisory Council or the management of the Phospholipid Research Center guided these expert groups.

Overview of some highlights:

Dermal Application of Phospholipids

"Electro-Spun Bioactive Wound Dressing", an innovative and promising technology using Phospholipids to improve formulation properties, presented by Francis Kamau Mwiiri and Prof. R. Daniels (University Tübingen, Germany).

"Investigation of Liposomal Transdermal Drug Delivery by Raman Microscopic Imaging in Combination with Stable Isotopic Labelling as a New Non-Invasive Modality to Study Drug Penetration", given by Dr. Anna Mühlig (Dr. C. Matthäus, University Jena, Germany). Their study was an exciting extension to results presented in the seminar of D. Gutekunst obtained with lipidomic analysis, used to track the skin interaction of phospholipid-based formulations.

Oral Application of Phospholipids

Oral administration is still the most important route for drug application. Marina Kolbina (Prof. R. Bodmeier, Freie Universität Berlin, Germany) were of special interest to explore the knowledge on the utilization of phospholipids and new dosage forms "Extruded Phosphatidylcholine Matrices for Oral Controlled Delivery". Maryam Farzan (Prof. J. Huwyler, University Basel, Switzerland) highlighted other novel oral applications of phospholipids by using phospholipids in combination with porous carriers.

Parenteral Application of Phospholipids

The parenteral route is still the most important route of application for phospholipids. Therefore, it is logical that the highest number of research projects came from this area. The potential of Phospholipids is impressive, when considering t the presented technologies in the seminars on "Polymer-Bounded Nanodiscs as Phospholipid Carriers" (Prof. S. Keller, University Kaiserslautern, Germany) and "Lipid Phase Behavior of Phospholipid-Coated Ultrasound Contrast Agents" (Simone Langeveld, Prof. K. Kooiman, Erasmus MC, Rotterdam, The Netherlands).

The meeting closed with a summarizing discussion. Each expert group outlined the acquired knowledge and presented the remaining questions and issues in front of all participants. Some open issues that ask for further investigations acted as take home messages and stimulated further discussions during the following dinner. These were e.g. the still lacking in vivo evidence for oral bioavailability enhancement by phospholipids or the lack of attention paid to phospholipids as emulsifier in parenteral emulsions.

Upcoming Events

July 21st–24th, 2019

46th Annual Meeting & Exposition of the Controlled Release Society

Valencia, Spain

46th Annual Meeting & Exposition of the Controlled Release Society
The Phospholipid Research Center will give a special workshop at the 46th Annual Meeting of the CRS in Valencia, Spain on July 21st–24th, 2019. Reputed scientists in the field of phospholipid research will give lectures at this event, like:
Prof. Y. Barenholz, Hebrew University, Israel
Prof. G. de Rosa University Federico II of Naples, Italy
Prof. A. Fahr University Jena, Germany
Prof. J. Kuntsche University of Southern Denmark
Prof. P. Luciani University Jena, Germany
Prof. M. Küntz University of Applied Sciences and Arts, Switzerland
PD Dr. P. van Hoogevest PRC

We look forward to meet you there!

September 9th–10th, 2019

6th International Symposium on Phospholipids in Pharmaceutical Research

Heidelberg, Germany

6th International Symposium on Phospholipids in Pharmaceutical Research
The Phospholipid Research Center will invite to the 6th International Symposium on Phospholipids in Pharmaceutical Research on September 9th–10th, 2019 in Heidelberg, Germany. The versatility of phospholipids and latest advances in industrial and academic research on phospholipid-based formulations and products are the focuses of this event. Our intension is to offer a platform for discussion and contact between academia, industry and regulatory authorities throughout all areas of interests of phospholipid scientists and formulators.

As in the previous events too, we invited speakers from industry and academia who are experienced in the research with phospholipids and development of phospholipid based dosage forms.

Some highlights will be the seminars given by:
Ass. Prof. J. Jun-Pil, Chosun University, College of Pharmacy, Republic of Korea
Prof. P. Luciani, Friedrich-Schiller University Jena, Germany
Dr. H. Han, HERON Therapeutics Inc., USA
Dr. C. Klose, Lipotype GmbH, Germany
Prof. A. Schroeder, Technion Research & Development Foundation Ltd., Israel
And many more …

Young scientists from all over the world will also make a significant contribution to the scientific content of the symposium. They are encouraged to present their latest findings in short presentations and/or on a poster. The submission deadline will be announced at the beginning of 2019.

Lipid Analytics

Analysis of Phospholipids in Bio-Oils and Fats by Hydrophilic Interaction Liquid Chromatography-Tandem Mass Spectrometry

A sensitive and selective liquid chromatography–electrospray ionization–tandem mass spectrometric (LC–ESI-MS/MS) method was developed for simultaneous (semi)-quantification of a very large array of Phospholipid (PL) classes in bio-oils and fats. The method applies Hydrophilic Interaction Liquid Chromatography–scheduled Multiple Reaction Monitoring (HILIC–sMRM) and zwitterionic HPLC column for efficient separation of 14 PL classes (Figure 2) and to obtain a dynamic range of more than six orders of magnitude. Eight PL class-specific internal standards (homologs) and more than 400 scheduled MRMs are employed for the measurement of PLs in a run time of 34 min. The method's performance was evaluated for vegetable oil, animal fat and algae oil. The averaged within-run precision and between-run precision were ≤10 % for all of the PL classes that had a direct homologue as an internal standard. The method accuracy was generally within 80–120 % for the tested PL analytes in all three sample matrices. The work and the method are described in detail in J. Viidanoja, J. Chromatogr. B 1001 (2015) 140–149.

A variety of oils and fats are typical raw materials for the production of renewable diesel fuels. The raw materials include different types of vegetable oils (1st generation biofuel raw materials), wastes, residues, and side streams (2nd generation biofuel raw materials), such as Animal Fats (AF), Used Cooking Oil (UCO) and Palm Fatty Acid Distillate (PFAD), as well as 3rd generation biofuel raw materials, such as algae oil. In the renewable diesel manufacturing process (Neste NEXBTL diesel), oils and fats are catalytically hydrogenated. The final product is mostly composed of alkanes that originate from fatty acyls of different glycerolipids, mainly mono-,di- and triacylglycerides and free fatty acids. In addition to these lipids, oils and fats contain varying amounts of other lipids, such as phospholipids (PL), which contain phosphorus in their phosphate group.

Catalysts are required in the hydrodeoxygenation (HDO) and isomerization steps. Phosphorus is a catalyst poison. Therefore, PLs must be removed from the feedstock using different pretreatment processes, such as degumming and bleaching. The suitability of the feedstock for the manufacturing process and the efficiency of the pretreatment processes can be evaluated by quantifying PLs in each PL class.

Concentrations of PLs in bio-oils and fats can vary by four orders of magnitude, from <1 mg/kg (purified/pretreated materials) to several thousands of milligrams per kilogram (algae oils). In addition, the PL distribution can vary great within and between the phospholipid classes. As a result, the concentration of individual PL species vary by more than six orders of magnitude. To attain such a wide dynamic range in an analytical method, both adjustable sample preparation and detector that provides both wide dynamic range and high selectivity are required.

Bio-oil samples cannot injected directly into the HPLC column, the sample matrix has to be removed first because they contain interfering high amounts of other lipids, mainly acylglycerides and free fatty acids. Generally, it is done with Solid Phase Extraction (SPE) and by retaining the PLs on the SPE column while the matrix is washed away. Diprotic PLs, phosphatidic and lysophosphatidic acid may exist in oils in Mg and Ca metal chelate forms. To ensure that they are retained in SPE and later in chromatography as expected, citric acid is added to the sample to break the chelates prior to SPE. Various sample dilution steps are performed before SPE to avoid overloading the SPE cartridge and detector with PLs and other highly retaining lipids. The correct dilution factor for sample dilution can be determined based on the initial phosphorus content of the sample that is determined separately with another method. The Internal standard (IS) concentration in the sample solution is kept constant, irrespective the dilution factor because method performance (sensitivity) may otherwise deteriorate. →

This also allows IS signal intensity to be used as Quality Control (QC) metrics for SPE recovery and LC-MS performance. This is especially important when the method is used for the analysis of diverse range of sample matrices of variable complexity and lipid composition, several of them not necessarily included in the method validation. In addition, IS intensity is preferred to be similar in the sample and in calibration standards even if calibration curves are seemingly linear.

PLs in oils and fats have traditionally been measured using high-performance liquid chromatography (HPLC) with ultraviolet (UV) or evaporative light scattering (ELSD) detection. These techniques are excellent for high concentrations and for the specific analytical problems for which they were created. However, they have limited selectivity and sensitivity and cannot provide universal solution for wide range of lipid profiles and concentrations.

Liquid chromatography tandem mass spectrometry (LC–MS/MS) and direct-infusion tandem mass spectrometry (MS/MS), the so-called shotgun lipidomics approach, offer more universal solutions for PL analytics. Due to the MS/MS overlap, certain PL species of phosphatidylcholines (PC) and sphingomyelins (SM) may not be distinguished from each other without LC. LC–MS/MS also yields better sensitivity and detection of minor components than the shotgun approach due to the sequential ionization of the analytes. Measurement sensitivity is further improved by removing most of the sample matrix with SPE prior to LC–MS/MS (matrix effects reduced or omitted). In order to monitor hundreds of MS/MS transitions in a single LC-MS method and simultaneously to have reasonable MS/MS sensitivity (MS/MS duty cycle), MS/MS operation has to be scheduled. In scheduled Multiple Reaction Monitoring (sMRM) individual MS/MS transitions are monitored only within time window where compounds elute out of the LC column.

Because PLs are polar and non-volatile, electrospray ionization (ESI) has to be employed in conjunction with MS. In practice, ESI requires internal standards (ISs) for quantitative analysis due to its susceptibility to matrix effects and temporal signal variation. Bio-oils can typically contain tens to hundreds of PL species, and their identity varies between sample types. It is practically impossible to have separate calibration curves and internal standards for each PL species. However, individual PL species possess similar response factors within acyl carbon and double bond range bio-oils typically have. Therefore, calibration with PL standards which acyl carbon number is similar to the analytes, leads to quantitative results, when the experimental conditions are carefully selected.

By default, calibration standards should be run and calibration curves generated in LC-MS every day samples are being run. However, this is not needed if Relative Response Factors (RRFs) (i.e. the ratio of response of the analyte to the IS) do not change over time. This is more likely the more similar the analyte and IS are. At best the IS is a stable isotope analog of the analyte but applying closely related homolog as an IS can also lead to relatively stable RRFs. In that case, instead of reproducing calibration curves every day, a sound calibration may be applied. It is created by running calibration standards on multiple days and combining them into a single calibration. Stability of the RRFs and validity of the approach should be evaluated for example by studying how much daily calibration curves deviate from each other (accuracy of calibration). If approach is considered accurate enough validity of fixed calibration is verified for each run by running reference sample and confirming that measured concentration is within acceptance limits from the value assigned when calibration was generated or method was validated. The need for applying fixed calibration in case of PLs stems from the challenges in preparing, ensuring and maintaining accurate and stable calibration solutions. These practical issues can be a larger risk for maintaining accurate calibration than inherent stability of RRFs. →

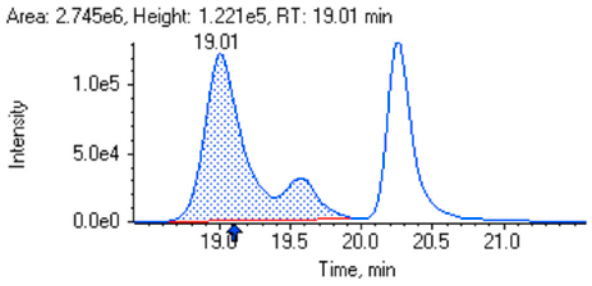


Figure 1: Good peak shape and chromatographic separation was obtained for three isomers of LPA 20:4 (457/153 MS/MS selected ion chromatogram).

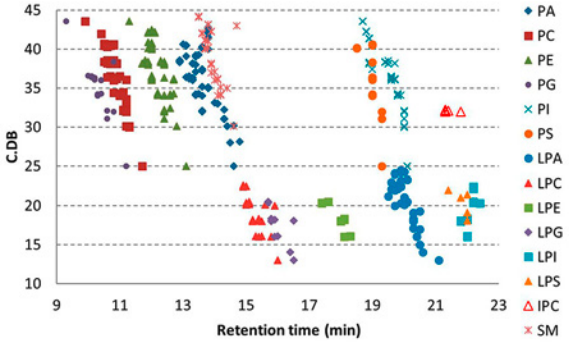


Figure 2: Retention times of phospholipids as a function of the amount of fatty acyl carbons (C) and double bonds (DB) in the molecule.

In practice, it is very challenging to obtain a good chromatographic peak shape and chromatographic separation simultaneously for a large array of PL classes. One of the most challenging PL classes for obtaining a symmetric peak shape without tailing is LPA (Figure 1).

Excellent separation of 14 PL classes (Phosphatidic acid (PA), Phosphatidylcholine (PC), Phosphatidylethanolamine (PE), Phosphatidylglycerol (PG), Phosphatidylinositol (PI), Phosphatidylserin (PS), Lyso-PA, (LPA), Lyso-PC (LPC), Lyso-PE (LPE), Lyso-PG (LPG), Lyso-PI (LPI), Lyso-PS (LPS), Inositolphosphoceramide (IPC) and Sphingomyelin (SM)) was obtained with the HILIC method (Figure 2).

In addition to good peak shape, it is important that the PL classes that produce the same fragment ion (Q3 ion) or the same neutral loss (60 amu for PC and SM) do not co-elute because of an increased risk of measurement interference. This requirement was fulfilled by the method for all of the PL classes, except for PIs that co-elute with LPA (Figure 1). However, because LPA is a lyso species and has a small phospholipid head group, while PI has a large head group, these two PL classes have very different Q1 masses and can be discerned from each other based on Q1 mass.

In the Hydrophilic Interaction Liquid Chromatography (HILIC), retention of PLs on the HPLC column is based on interactions between the polar PL head groups and polar stationary phase, while the structure of fatty acyls, including the amount of fatty acyl carbons and double bonds, plays a minor role in the retention. Thus, the PLs of the same PL class elute out of the column at approximately the same time interval. The great benefit of this is that it enables the use of PL class-specific internal standards that have the same head group and number of fatty acyl groups as the analytes and which elute within the same time range as the PL analytes of the class. Therefore, it can be expected that the analytes and the lipid class-specific IS experience similar ionization conditions (ESI matrix effects and temporal signal variation). The resulting signal normalization by IS is the basis of quantitative measurement, when ESI is applied.

Many PL classes can be measured either in the positive or negative mode by monitoring the protonated or deprotonated molecules or various adducts. The negative ion mode was selected for the method because it allows for the measurement of all of the PL classes, including PA and LPA, in the same run without applying polarity switching. The measurement of PC, PE, LPC and SM would have been more sensitive in the positive mode, but because PC and LPC were the dominant PL classes in almost all of the tested bio-oils, measurement of PC or LPC in the positive mode would have resulted in larger dilution factors to avoid detector saturation, which would have also compromised the sensitivity of the measurement for several other PL classes. →

Before selecting the IS and IS MS/MS transitions to be used in the method a large number of different bio-oils and fats were analyzed to identify commercially available IS candidates that have negligible ion background in sample MS/MS spectra (within the target sMRM window). This is critical to avoid (negative) bias in quantification, due to sample component signal being added to the IS signal. This excluded the PLs with 17:0/17:0 and lyso PLs 17:0 fatty acyl chains that are typically used as IS in lipidomic experiments because species with the same Q1 and Q3 masses were detected in several sample matrices. One or two IS candidates were selected per PL class for method accuracy evaluation. Due to the limited availability of IS candidate materials and to limit the complexity and the number of IS in the method, the IS of PE, PG and PI were evaluated as the IS for the corresponding lyso species. PC IS was evaluated as the IS for SM. It was acknowledged that as a result of this, the measurement of these lyso species might not be as quantitative as the measurement of the other PL classes.

Further details on the method parameters, method development and validation can be found in J. Viidanoja, J. Chromatogr. B 1001 (2015) 140–149. Briefly, the analytical performance and suitability of the method for the intended purpose were assessed by method validation which included studying the linearity, precision (within run and between runs), accuracy and LLOQ separately for three different sample matrices, namely: Soya Bean Oil (SBO), Animal Fat (AF) and Nannochloropsis oculata algae oil (1st, 2nd and 3rd generation biofuel raw material, respectively). Precision was determined by analyzing four replicates of each sample on three days using two different injection volumes. Accuracy was determined by spiking studies (four concentration levels) using from one to two different ISs and the same analytes as those used for instrument calibration. The validation was termed partial because full validation was impossible due to practical limitations (only limited number of pure analytes standards are available and can be included in the validation. The validation could be done only with limited set of sample matrices).

The calibration curves were found to be linear over three orders of magnitude. The averaged within-run precision and between-run precision were generally ≤10 % for all of the PL classes that had a direct homologue as an IS and the concentration was ≥1 mg P/kg. Accuracy was generally within 80–120 % for all the three sample matrices, indicating that ISs and analytes behaved similarly in SPE and ISs corrected possible ESI matrix effects. Based on these results it can be concluded that the hydrophilic interaction liquid chromatography–tandem mass spectrometry method is suitable for quantitative analysis of broad range of phospholipids from diverse and complex sample matrices.

Jyrki Viidanoja*
Technology Centre, Kilpilahti,
Neste Corporation, P.O. Box 310,
FI-06101 Porvoo, Finland

*Present address:
Thermo Fisher Scientific,
Ratastie 2
FI-01620, Vantaa
Finland.
Jyrki.Viidanoja@gmail.com

PUBLISHER

Phospholipid Research Center

EDITOR

Dr. Peter van Hoogevest
Co-editor Dr. Dorothea Gutekunst
Featuring authors Dr. Jyrki Viidanoja

LAYOUT AND DESIGN

Ina von Jeinsen

CONTACT

Phospholipid Research Center

Im Neuenheimer Feld 515
69120 Heidelberg, Germany

Phone: +49 (0)6221 / 588 8360
Fax: +49 (0)6221 / 651 5665
E-Mail: info@phospholipid-institute.com
www.phospholipid-institute.com

Phospholipid Research Center

Im Neuenheimer Feld 515
69120 Heidelberg, Germany

Phone: +49 (0)6221 / 588 8360
Fax: +49 (0)6221 / 651 5665
E-Mail: info@phospholipid-institute.com

www.phospholipid-institute.com