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The 8th International Symposium on Phospholipids in Pharmaceutical Research – An update on current research in phospholipids presented at the biennial symposium of the Phospholipid Research Center Heidelberg[1]

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ABSTRACT

This *Conference Report* recaps recent advances in the research on phospholipids and their applications for advanced drug delivery and analytical purposes that have been presented at the *"8th International Symposium on Phospholipids in Pharmaceutical Research"* of the Phospholipid Research Center (PRC), held from September 09–11, 2024, at the University of Heidelberg, Germany. The PRC is a non-profit organization focused on expanding and sharing scientific and technological knowledge of phospholipids in pharmaceutical and related applications. This is accomplished by, *e.g.*, funding doctoral and postdoctoral research projects at universities worldwide. The PRC organizes this symposium every two years, at which international experts from science and industry present innovative and new applications of phospholipids. This year's symposium highlighted advancements in lipid-based gene and RNA delivery, anisotropic lipid nanoparticles, PEGylation challenges, tetraether lipids for drug delivery, ethical considerations in publishing, multifunctional lipopeptides, and phospholipid applications in therapeutics. Discussions also showcased award-winning research on optimizing liposome drug compatibility, reflecting the expanding role of phospholipids in pharmaceutical science.

1. The 8th International Symposium on Phospholipids in Pharmaceutical Research

The Phospholipid Research Center (PRC) hosted its biennial International Symposium for the eighth time from September 09–11, 2024, in Heidelberg, Germany. The two-and-a-half-day conference with 140 participants was organized into seven sessions covering different aspects and recent advances in the research on phospholipids and their applications for drug delivery and analytical purposes. The aim of the symposium was to foster the dialogue between different academic researchers and institutes about the role of phospholipids in different pharmaceutical applications and basic research.

Topics included discussions on innovative strategies in lipid-based gene and RNA delivery, novel perspectives on anisotropic nanoparticle systems and PEGylation challenges, the application of tetraether lipids in advanced drug delivery, ethical considerations in publishing alongside nanotechnology-driven therapeutics, advances in lipid-based formulations and multifunctional lipopeptides, cutting-edge phospholipid applications in therapeutic interventions, and award-winning innovations in liposome drug compatibility.

The objective of this *Conference Report* is to recap the lectures and to highlight the role of phospholipids in the different applications and research.

2. The beauty of phospholipids

The molecular structure of phospholipids comprises a glycerol backbone which is esterified in positions 1 and 2 with lipophilic (hydrophobic) fatty acids and in position 3 with a hydrophilic phosphate or phosphate ester, respectively. They represent a class of versatile biomolecules that for application purposes are primarily derived from natural sources such as soybean, sunflower, and hen egg yolk. Their amphiphilic nature confers them unique physicochemical properties, which underpin a broad spectrum of biological and technological functions (Drescher and van Hoogevest, 2020; Wibel et al., 2024).

In nature, the major role of phospholipids is the formation of cellular

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membranes by organizing into lipid bilayers into which proteins are incorporated or peripherally bound. This structural arrangement is essential for the stability and functioning of cells and intracellular membranes. Beyond cell membranes, phospholipids are key components in various physiological contexts; they are present in bile, incorporated in lipoproteins, contribute to the mucosal linings (for example, as lung surfactant), and participate in bone formation within the lipid-calcium-phosphate complex (Hanin and Pepeu, 1990; Merolli and Santin, 2009; Vertzoni et al., 2012). Additionally, phospholipids serve as important reservoirs of essential fatty acids and therefore energy. They are actively involved in critical biochemical processes such as the regulation of blood coagulation (Lentz, 2003) and apoptosis (Devitt et al., 2003). Owing to their low toxicity profile, these molecules are well-suited for pharmaceutical applications using various routes of administration, which significantly enhances their utility (van Hoogevest et al., 2021).

The inherent structural diversity of phospholipids facilitates their incorporation into numerous pharmaceutical formulations. They are not only used as natural emulsifiers, wetting agents, and solubilizers, but also serve as essential matrix materials for the development of advanced drug delivery systems such as liposomes, lipid nanoparticles (LNPs), and mixed micelles (van Hoogevest et al., 2021; van Hoogevest and Wendel, 2014; van Hoogevest, 2017; van Hoogevest and Luciani, 2018; van Hoogevest and Fahr, 2019; van Hoogevest, 2020). Recent breakthroughs have further highlighted their importance in the formulation of LNPs, particularly for the delivery of therapeutic nucleic acids such as siRNA and, for vaccination purposes, mRNA (Mendonça et al., 2023) during the COVID pandemic.

Given their remarkable versatility and inherent advantages, ranging from biocompatibility and biodegradability to their critical roles in cellular and systemic functions, the potential for novel applications of phospholipids remains extensive. This conference report aims to not only underscore their established benefits but also to shed light on the current innovative research initiatives conducted by the PRC, which continue to expand the horizons of pharmaceutical sciences (Wibel et al., 2024).

3. Innovative strategies in lipid-based gene and RNA delivery

The first session showcased cutting-edge developments in the field of lipid-mediated delivery systems for gene therapy and RNA-based therapeutics, emphasizing novel targeting strategies and the integration of both synthetic and biological approaches.

Advances in Gene Delivery Platforms. The first presentation, given by Christian Buchholz (Buchholz, 2024), provided an insightful overview of the current boom in gene therapy, where both viral vectors and LNPs are central to therapeutic advancements (Mendonça et al., 2023). The discussion focused on the engineering of gene delivery vehicles, where natural receptor interactions are modified, *via* point mutations and the attachment of high-affinity binders such as designed ankyrin repeat proteins, to achieve selective cell targeting. This strategy not only enhances delivery specificity for treatment-relevant cells (for instance, in cancer immunotherapy and the targeting of HIV reservoirs) but also opens avenues for *in vivo* generation of therapeutic cells. The work highlighted that achieving precise dual-receptor targeting (through bi-specific approaches) could mark a significant step forward in the efficacy and safety of gene therapy applications (Michels et al., 2022).

Extracellular Vesicle-Inspired RNA Delivery. The lecture by Pieter Vader (Vader, 2024) explored the potential of extracellular vesicles (EVs) as superior vehicles for RNA delivery. By employing a novel CRISPR/Cas9-based reporter system, the presenter demonstrated that EVs can deliver RNA at efficiencies several orders of magnitude higher than conventional LNPs. To address challenges in RNA loading, the research introduced hybrid nanoparticles that combine EVs with liposomes, thereby merging the advantages of biological and synthetic delivery systems for siRNA. Additionally, the adaptation of EVs for the delivery of CRISPR ribonucleoproteins was presented as a promising approach for precise gene editing. These findings are supported by recent studies on EV-mediated communication and functional RNA transfer (de Jong et al., 2020; van Niel et al., 2022).

Targeting Lipid-Based Carriers to Myeloid Cells. The last contribution in this session, given by Daryl Drummond (Kirpotin et al., 2024), focused on the targeted delivery of lipid-based formulations to key immune cells, including macrophages, monocytes, and dendritic cells. A notable example discussed was a minimally PEGylated liposomal formulation designed for irinotecan, which, through sustained release and localized conversion to its active metabolite, has shown remarkable efficacy in treating metastatic pancreatic cancer. The presentation further described the development of liposome-encapsulated antibiotics aimed at intracellular pathogens in tuberculosis and the design of ligand-directed LNPs that enhance the delivery of mRNA to dendritic cells, thereby significantly improving transfection rates and immunogenicity for vaccine applications.

Overall, the session underscored the versatility and promise of lipid-based delivery systems, highlighting that continued innovation in vector engineering, hybrid nanoparticle design, and targeted delivery can substantially advance therapeutic outcomes for a range of diseases where therapies prove to be challenging.

4. Novel perspectives on anisotropic nanoparticle systems and PEGylation-related challenges

The second session explored innovative strategies in the design of phospholipid-based drug delivery systems, focusing on the benefits of anisotropy and addressing critical safety concerns associated with PEGylation.

Anisotropic Phospholipid-Based Delivery Systems. The presentation by Vincent Faivre (Faivre, 2024) delved into the potential of anisotropy in nanometric and micrometric particles to enhance drug delivery. The discussion highlighted two distinct particle architectures. The first involved compositionally anisotropic particles with dual compartments, one hydrophilic and one hydrophobic, enabling the simultaneous encapsulation of therapeutic agents and diagnostic markers (Kudryavtseva and Sukhorukov, 2024; Truong-Cong et al., 2018). The second concept addressed elongated, non-spherical particles, which exhibit unique mobility and interactions with biological tissues that could offer advantages over conventional spherical particles (Lipa-Castro et al., 2021). These approaches underline how manipulating particle geometry and composition can improve encapsulation efficiency and targeting capabilities.

Unintended Immunological Effects of PEGylation. Another talk in this session, given by Janos Szebeni (B.A. Barta et al., 2024), examined the unforeseen immunogenic challenges associated with PEGylated nanoparticles. Although coating nanoparticles with polyethylene glycol (PEG) is commonly employed to stabilize formulations and prolong circulation time, the presence of pre-existing anti-PEG antibodies can provoke severe hypersensitivity reactions. Experimental data from a porcine model demonstrated that even a single intravenous injection of low-dose PEGylated liposomes induced a substantial and rapid increase in anti-PEG IgM levels, with these antibodies rapidly binding to the nanoparticles and triggering complement activation *via* the classical pathway (B.A. Barta et al., 2024; Kozma et al., 2019). The subsequent activation of the complement cascade was linked to immediate anaphylactic shock and pulmonary hypertension, suggesting that complement activation plays a key role in these adverse responses. These findings propose that monitoring complement activation may serve as a predictive model for assessing the safety of PEGylated nanomedicines (Kozma et al., 2023).

Overall, the session emphasized both the promising advancements in anisotropic lipid-based delivery systems and the critical need to understand and mitigate the immunological risks associated with PEGylation.

5. Tetraether lipids – from extremophile membranes to innovative drug delivery platforms

This session, devoted exclusively to tetraether lipids (TELs), captivated the audience with its in-depth exploration of these extraordinary biomolecules and their emerging pharmaceutical applications. The five sequential talks not only provided a comprehensive overview of the unique properties of TELs but also spurred enthusiastic discussions among attendees.

Exploring the Unique Chemistry of Archaeal Lipids. The opening lecture by Alexander Treusch (Treusch, 2024) explored the biology of extremophilic microorganisms, highlighting how their membrane lipids, featuring ether bonds instead of the classical ester linkages and membrane-spanning properties, confer exceptional stability under harsh conditions (S.M. Jensen et al., 2015). Both diether and tetraether lipids were discussed, emphasizing their resistance to extreme pH and digestive enzymes. These characteristics render TELs highly attractive for biotechnological applications, such as stabilizing nanoparticulate carriers for enhanced oral drug delivery (Jacobsen et al., 2017; Jensen et al., 2015).

Enhancing Nucleic Acid Delivery with TELs. Building on the discussion of lipid chemistry, the next presentation, given by David Wurm (Wurm et al., 2024), examined the incorporation of both native and semi-synthetic ionizable TELs into LNPs for mRNA delivery. By substituting conventional helper lipids with glycerol dialkyl glycerol tetraether lipids (GDGT) and newly developed ionizable lipids, significant improvements *in vitro* transfection efficiency were observed. *In vivo* studies further provided encouraging data on pharmacokinetics, toxicity, and storage stability (Sedlmayr et al., 2023, 2024).

TELs in Oral mRNA Vaccination Platforms. The third talk by Dagmar Fischer (Fischer, 2024) introduced an innovative carrier system for the oral administration of mRNA vaccines. This approach harnesses acid-stable TELs to protect the mRNA payload during gastrointestinal transit, ensuring safe and efficient delivery to the intestine. The process included optimizing archaeal cultivation for large-scale TEL production and varying the lipid headgroups to establish structure–function relationships, resulting in a platform that could simplify manufacturing and reduce costs—an aspect particularly beneficial for developing countries (Rastadter et al., 2020; Scholte et al., 2021).

Advancing Oral Peptide Therapeutics with TEL-Based Liposomes. Addressing the challenge of oral peptide delivery, the fourth talk presented by Philipp Uhl (Uhl et al., 2024) showcased a liposomal nanocarrier that integrates TELs with cell-penetrating peptides (CPPs). The exceptional stability conferred by TELs enables these carriers to withstand the gastrointestinal environment, while CPPs enhance mucosal uptake. Preclinical studies in rodents and higher mammals demonstrated markedly improved oral bioavailability of a model peptide, suggesting potential for broader applications in delivering peptide therapeutics, including those targeting multidrug-resistant pathogens (Uhl et al., 2021, 2023; Werner et al., 2024).

Synthetic Alternatives to Natural TELs. The final lecture, given by Simon Drescher (Drescher, 2024), addressed the feasibility of synthetic TELs as substitutes for naturally derived counterparts. By comparing the structural hallmarks, such as the invers *sn*-2,3 glycerol configuration, ether-linked isoprenoid chains, and branched methyl groups, this talk evaluated both the synthetic challenges and potential pharmaceutical advantages of simplified TEL analogs. Two main strategies were discussed: extraction from archaea *versus* chemical synthesis with simplified chemical structures, the latter aiming to reduce complexity while retaining key functional attributes for liposome stabilization (Drescher et al., 2007; Gruhle et al., 2018; Markowski et al., 2014; Müller et al., 2019).

Overall, this session not only highlighted the remarkable adaptability of TELs in overcoming formulation challenges but also demonstrated their broad potential to revolutionize drug and vaccine delivery. The enthusiastic response from the audience underscores the significant interest in TEL-based innovations within pharmaceutical research.

6. Emerging frontiers in scholarly publishing and nanotechnology-driven therapeutics

The first session of the second day explored a diverse range of topics, spanning from the transformative impact of generative AI on scholarly publishing to cutting-edge nanoparticle platforms for targeted therapeutic applications. The session featured two invited talks and two selected short presentations, each contributing unique insights while collectively fostering a stimulating discussion.

Advances in Ethical Publishing in the Age of Generative AI. The session opened with an invited talk by Christine Mayer (Mayer, 2024) that examined the emerging role and the dangers of generative artificial intelligence (AI) in scholarly publishing. The speaker provided a comprehensive overview of how AI-driven tools can enhance efficiency and accessibility across all stages of the publishing process, from initial idea generation to long-term archiving. The presentation also highlighted new ethical challenges and risks, including copyright infringement, evolving definitions of authorship, and the traceability of AI-generated content, thus outlining the complex ethical landscape now facing the industry.

Selected Short Talks on Innovative Nanoparticle Applications. Following this, two concise presentations showcased innovative nanoparticle applications in therapeutic contexts. The first short talk by Christos Tapeinos (Tapeinos and Yang, 2024) introduced plasma membrane-derived nanoparticles as a promising strategy for targeted drug delivery across the blood-brain barrier (BBB). The research demonstrated that these nanoparticles can be selectively internalized by various cell types without compromising the barrier's integrity, and that loading them with an anti-inflammatory inhibitor effectively reduces pro-inflammatory markers in microglia. The work, supported by detailed *in vitro* studies, points toward potential applications in treating glioblastoma and other neuroinflammatory conditions (Tapeinos et al., 2023).

In the second short presentation, Simon Matoori (Matoori, 2024) described a novel liposomal microreactor for rapid lactate sensing in whole blood, a development with significant implications for bedside diagnostics in sepsis. By encapsulating the lactate detection reaction within a liposome that shields it from interfering blood components, the system achieved a linear response within two minutes over a clinically relevant range. The assay's performance was validated both in human capillary blood and in septic animal models, offering a promising route toward a fast, point-of-care diagnostic tool. This work builds on recent advances in liposomal sensor design and integrates near-infrared fluorescence for robust detection (Matoori and Mooney, 2020, 2022) and supporting work on portable fluorometry (Guirguis et al., 2023).

Nanotechnology Approaches in Ophthalmologic Therapeutics. The session concluded with an invited talk by Félix Sauvage (Sauvage et al., 2024) presenting a novel nanotechnology-based approach for treating vitreous opacities in the eye. Traditional treatments for floaters, such as YAG laser therapy or vitrectomy, have limitations and risks. Here, the speaker introduced a method that leverages the plasmonic properties of nanoparticles to generate vapor nanobubbles upon pulsed-laser irradiation, mechanically fragmenting collagen aggregates. Recognizing the non-biodegradability of conventional gold nanoparticles, the research explored the encapsulation of indocyanine green within liposomes to enhance safety by prolonging residence time in the vitreous body while reducing retinal penetration. Preliminary *in vivo* studies in rabbit models indicate that hyaluronic acid-coated liposomes may offer an effective and safer alternative for the photo-induced ablation of vitreous opacities (Sauvage et al., 2019) and subsequent *in vivo* findings (Sauvage et al., 2022).

Overall, the session bridged diverse fields, from the ethics of modern publishing in the era of AI to groundbreaking nanoparticle systems for drug delivery and diagnostics, stimulating lively discussion and offering

new perspectives on both technology and clinical application.

7. Innovations in biologics stabilization and nanoparticle production and characterization

This session provided a multifaceted view on modern strategies in biologics formulation and nanoparticle characterization, featuring an invited talk, two selected short presentations, and two technical spotlights.

The session opened with an invited presentation, given by Wolfgang Frieß (Frieß and Papadopoulos, 2024), addressing the challenges of stabilizing therapeutic proteins formulated in aqueous solutions. The speaker explored the use of lysophosphatidylcholines (LPCs) as alternative surfactants to conventional polysorbates (PS), which are prone to hydrolysis and oxidation. The research demonstrated that LPCs form elastic films at interfaces, effectively displacing protein molecules and preventing aggregation. At concentrations above 0.01 mg/ml, these surfactants cover the interface completely, thereby protecting the protein from interfacial stress, while exhibiting lower degradation tendencies even after lyophilization. Overall, LPCs showed comparable interfacial stabilization properties to PS, suggesting a promising alternative for parenteral protein formulations (Papadopoulos et al., 2024).

Two short presentations followed, both contributing valuable insights into nanoparticle systems. One study, presented by Dayana Benkova (Benkova et al., 2024), investigated the interactions between chitosan-based hybrid nanomaterials and biomimetic cell membranes. By examining large and giant unilamellar vesicles that mimic different lipid phases, the research revealed that these nanomaterials increase membrane molecular order and induce morphological transformations, such as vesicle adhesion, fusion, and shrinkage. These findings shed light on the underlying molecular mechanisms governing the interactions between chitosan nanomaterials and lipid membranes, which could have significant implications for targeted drug delivery (Assa et al., 2017; Li et al., 2018).

In a complementary short talk, given by Annabelle Dietrich (Dietrich et al., 2024), a novel reversed-phase charged aerosol detection (RP-CAD) method was introduced for lipid quantification in LNPs. This approach enabled a detailed evaluation of process parameters during microfluidic mixing, revealing that deviations in lipid content can be attributed to the preparation of lipid stock solutions and small-scale dialysis, rather than the mixing flow rate. The methodology sets a new benchmark for process characterization in LNP manufacturing, with potential applications in other nanoparticle production processes (Fan et al., 2021; Weber et al., 2020).

The session concluded with two technical spotlights that showcased cutting-edge methodologies. In the first spotlight, Ulrich Massing (Bender et al., 2024) presented the dual asymmetric centrifugation (DAC) method as a rapid, sterile, and flexible technique for preparing liposomes and LNPs in small batches. This method, which combines impact and friction forces with adjustable parameters, allows precise control over vesicle size, lamellarity, and encapsulation efficiency, and holds promise for patient-specific, bedside nanoparticle preparation (Koehler et al., 2023). In the second spotlight, Nicolas Färber (Färber et al., 2024) introduced the Lipid State Observer (LISO), a temperature-controlled fluorescence spectroscopy tool that quantifies lipid order in liposomes and LNPs using dyes such as Laurdan. By measuring generalized polarization across a wide temperature range, LISO provides comprehensive insights into membrane fluidity, stability, and drug interactions, thus offering a valuable asset for formulation development and storage analysis (Farber and Westerhausen, 2022; Parasassi et al., 1991).

Overall, this session successfully bridged the fields of biologics stabilization and nanoparticle process characterization, sparking lively discussions on innovative approaches to overcome current formulation challenges and paving the way for future technological advancements in pharmaceutical development.

8. Advances in lipid-based formulations and multifunctional lipopeptides for enhanced drug delivery

The afternoon session commenced with an invited presentation by Heike Bunjes (Bunjes and Grüne, 2024) on phospholipid-based self--dispersing formulations designed to improve the bioavailability of poorly water-soluble drugs. The speaker explained how self-emulsifying lipid-based formulations, leveraging the amphiphilic properties and excellent tolerance of phospholipids, can be developed into liquid capsule filling materials. Various combinations of diacylphosphatidylcholines with triglyceride oils and fats were evaluated, revealing that formulations incorporating agents such as Phospholipon 90 G and Lipoid S 75 exhibit superior miscibility and dispersibility. Hard capsules made from hydroxypropyl methylcellulose were found to be more compatible with these formulations than gelatin capsules. The study also demonstrated that these systems provide good stability and acceptable drug loading for compounds with lower melting points, whereas drugs with higher melting points, like clofazimine, pose greater challenges (Grüne and Bunjes, 2020a, 2020b, 2024).

Following this, two selected short talks offered further insights into nanoparticle and membrane dynamics. In the first short talk, Cynthia Alsayyah (Alsayyah et al., 2024) presented a novel method for modulating the compressibility of large unilamellar liposomes by reversibly tuning their sterol content using methyl-β-cyclodextrin in a dialysis setup. This approach, monitored *via* a solvatochromic probe, allowed for reversible changes in membrane compressibility and induced corresponding effects on protein oligomerization, thus providing a valuable tool for investigating cholesterol's impact on membrane protein structure and function. In the second short talk, Radek Šachl (Šachl et al., 2024) described a model system inspired by SNARE proteins to enhance vesicle fusion, a process essential for effective intracellular drug delivery. By employing synthetic lipopeptides to mimic natural SNARE functions, the study revealed that the spatial arrangement of complementary peptides is crucial for initiating membrane fusion, offering insights that could significantly improve drug delivery efficiency (Mora et al., 2020; Koukalova et al., 2018).

The session concluded with an invited talk by a distinguished guest from China, Professor Tu (Tu and Jiang, 2024), whose presentation highlighted recent advancements in multifunctional lipopeptides as excipients in lipid delivery systems. He detailed the design and synthesis of peptide-modified phospholipids that enhance both the loading capacity and barrier penetration of lipid carriers. His work showcased dendritic lipopeptides that markedly improve transdermal delivery through efficient skin penetration, cellular uptake, and mitochondrial targeting, thereby enhancing therapeutic outcomes for conditions such as melanoma and hypertrophic scars. In addition, mixed-charged dendritic lipopeptides were demonstrated to overcome oral delivery barriers, significantly improving the bioavailability of macromolecular drugs like insulin. This talk underscored the potential of multifunctional lipopeptides to advance both transdermal and oral drug delivery, representing an important milestone in lipid-based formulation technologies.

9. Thudichum Life Award – celebrating pioneering advances in phospholipid research

This special session concluded the second day of the symposium on a high note with the presentation of the Thudichum Life Award to Professor Dr. Alberto Gabizon. The session began with a brief introductory lecture by Alfred Blume, who honored Johann Ludwig Wilhelm Thudichum, a visionary physician and biochemist renowned for isolating and characterizing brain compounds, including phospholipids. Thudichum's groundbreaking work laid the foundation for recognizing the physiological importance of phospholipids and set the stage for future advances in the field.

Following this tribute to Thudichum's legacy, Professor Gabizon was

formally recognized for his lifelong and outstanding contributions to phospholipid research. A leading figure in cancer therapy and liposomal drug delivery systems, Professor Gabizon is best known for his pioneering work on PEGylated liposomal doxorubicin (Doxil/Caelyx). Developed during his early career, this innovative formulation harnesses phospholipid-based technology to improve drug stability and enhance selective tumor accumulation, thereby revolutionizing targeted chemotherapy while minimizing side effects. His subsequent developments, including Promitil®, a PEGylated liposomal mitomycin-C prodrug, and the hybrid therapeutic PLAD, further exemplify his commitment to advancing cancer nanomedicine. In addition to his scientific achievements, Professor Gabizon's entrepreneurial spirit is reflected in the founding of two start-up companies aimed at translating his research into clinical applications. His distinguished career, marked by numerous accolades such as the Kaye Innovation Award and the Bangham Lifetime Achievement Award, underscores his profound impact on both research and patient care. Currently leading the Nano-oncology Research Center in Jerusalem, Professor Gabizon continues to push the boundaries of translational medicine, embodying the interdisciplinary spirit of Thudichum's heritage.

The Thudichum Life Award thus not only honors Professor Gabizon's exceptional contributions to phospholipid research and cancer therapy but also serves as an enduring reminder of the transformative power of innovative scientific inquiry.

10. Advanced applications of phospholipids in drug delivery and therapeutics

The morning session of Day 3 showcased three invited talks that underscored the expanding role of phospholipid-based systems in addressing diverse therapeutic challenges. The session brought together innovative approaches ranging from chronic liver disease management and intracellular protein delivery to the development of light-responsive drug release platforms.

Phospholipids in Chronic Liver Disease Management. In the first invited talk, Paola Luciani (Luciani, 2024) explored the potential of phospholipids in the treatment of chronic liver disease, particularly metabolic dysfunction-associated fatty liver disease. The research demonstrated that soybean-derived polyenylphosphatidylcholines can reverse liver fibrosis and mitigate oxidative stress. Furthermore, the speaker presented the development of a lipid mesophase-based ink designed for 3D-printed tablets. These tablets remain intact under acidic conditions but self-emulsify in intestinal fluids, thereby enhancing the solubility of poorly water-soluble drugs while maintaining cell viability. This innovative approach holds promise as an oral treatment strategy for chronic liver disease by delivering antifibrotic and bioactive agents effectively (Skorup et al., 2023; Carone et al., 2024).

Cardiolipin-Containing Liposomes for Intracellular Protein Delivery. In the second invited talk, Shiqi Wang (Wang et al., 2024) addressed the challenges associated with delivering large and complex protein drugs into cells. The research focused on the design of cardiolipin-containing liposomes co-loaded with a pro-apoptotic protein and a glycolysis inhibitor to promote apoptosome assembly and induce cancer cell apoptosis. The lipid formulation leveraged the complexation of cardiolipin with the protein, and the addition of a tumor-targeting peptide significantly enhanced specificity toward tumor cells, as demonstrated in both *in vitro* and *in vivo* models. This strategy highlights the potential of advanced liposomal formulations in overcoming intracellular delivery barriers for protein therapeutics (Chaudhary et al., 2021; Han et al., 2023; Morshedi Rad et al., 2021).

Light-Activated Drug Release from Liposome-Hydrogel Systems. In the final invited talk, Timo Laaksonen (Laaksonen, 2024) presented cutting-edge research on controlled and sustained drug release using light-responsive liposome-hydrogel systems. The work focused on integrating cationic liposomes within cellulose nanofiber hydrogels to form drug "nano-depots" capable of retaining their cargo for extended periods with minimal passive release. Two distinct light-activated release mechanisms were explored. In the first approach, a photosensitizer was employed to generate heat upon illumination at 808 nm, which increased liposome permeability and triggered drug release. The second approach utilized a pyridine-substituted zinc phthalocyanine to induce release *via* photothermal and photo-oxidation effects when activated by LED light at 730 nm. Detailed investigations into release parameters provided valuable insights for the design of advanced medical devices and implantable systems (Auvinen et al., 2020, 2022; Lem et al., 2024).

Overall, this session demonstrated the versatility of phospholipid-based platforms in addressing critical challenges in drug delivery and therapeutic interventions. The innovative approaches presented are paving the way for more effective, targeted, and patient-friendly treatments in the fields of liver disease, oncology, and controlled drug release.

11. Thudichum Young Scientist Award: advancing liposome drug compatibility

The symposium concluded with the Thudichum Young Scientist Award. In 2024, the award went to Dr. Martin Balouch from Prague, Czech Republic, in recognition of his innovative work on optimizing drug–liposome compatibility.

Dr. Balouch's study focused on the role of drug permeability and partitioning across phospholipid bilayers, using COSMOPerm calculations and fluorescent dye experiments. His findings enabled the classification of drugs into distinct groups, too permeable, membrane suitable, pH switchable, thermally releasable, and non-permeable, providing a predictive framework for liposome formulation. Additionally, his exploration of computational prodrug design, notably with fructose-adducts, revealed non-proportional changes in permeability that could improve liposome-based delivery systems (Balouch et al., 2021; Balouch et al., 2023).

12. Summary

The symposium provided a comprehensive overview of the latest advancements in phospholipid research, emphasizing their outstanding role in drug delivery, gene therapy, and pharmaceutical formulations. Discussions covered innovative lipid-based delivery systems, the optimization of nanoparticle properties, and strategies to overcome biological barriers. Novel approaches, including the use of tetraether lipids, multifunctional lipopeptides, and cardiolipin-containing liposomes, showcased the versatility of phospholipids in improving drug stability, bioavailability, and therapeutic targeting. Ethical considerations in scholarly publishing and emerging technologies for lipid characterization further underscored the evolving landscape of phospholipid science.

Beyond their application in drug delivery, the symposium highlighted the adaptability of phospholipids in a wide range of biomedical and pharmaceutical contexts. From controlled-release hydrogels and light-activated formulations to computational modeling for optimizing liposome compatibility, phospholipids continue to serve as fundamental building blocks for cutting-edge therapeutics. Their unique physicochemical properties allow for precise modulation of drug interactions, enabling advancements in personalized medicine and targeted treatments. The recognition of outstanding contributions through the Thudichum Awards reinforced the significance of continued research in this field, bridging fundamental discoveries with translational applications.

With phospholipids at the forefront of pharmaceutical innovation, the next symposium, scheduled for August 31 to September 2, 2026, will provide a platform for further groundbreaking research and collaboration. As new challenges and opportunities emerge, the event promises to foster scientific exchange and drive the next generation of phospholipid-based therapies.

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Simon Drescher: Writing – review & editing, Writing – original draft, Conceptualization. **Alfred Blume:** Writing – review & editing, Writing – original draft.

Declaration of competing interest

Simon Drescher and Alfred Blume declare no conflict of interest.

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