Transdermal & Intradermal Drug Delivery Systems 2017
Advanced Design, Development & Delivery of Skin-Mediated Therapies and Vaccines

FeaturedSpeakersInclude:

Thean Yeoh
Pfizer

Bobby Singh
Corium

Lisa Dick
3M

Mikolaj Milewski
Merck

Samir Mitragotri
UC Santa Barbara

Ryan Donnelly
Queens University

With Comprehensive Coverage On:

• Improving Bioavailability Via Transdermal Administration
• Latest Advances in Microneedle Drug and Vaccine Delivery
• How to Move from Passive to Active Skin-Mediated Delivery Technologies for Drugs and Biologics
• Optimizing TDD & IDD for Efficacious Delivery and Patient Compliance
• Computational Modeling of Transdermal and Intradermal Delivery

• Resolving Regulatory Compliance Issues for TDD & IDD Systems
• Mechanisms of Dermal and Transdermal Absorption of Drugs
• IVPT and IVRT of Transdermal and Topical Products
• Exploring the Promise of Ionic Liquids for Transdermal Applications
• And much more!

The growing interest in alternative routes of drug administration has experts predicting that the market for transdermal and intradermal drug delivery systems will exceed $25 billion in 2018. The industry is on the threshold of bringing into commercial production a new generation of transformative TDD and IDD therapies and delivery systems. That is why you cannot afford to miss this two-day intensive conference. Pharma Ed brings together leading researchers in the field to share the most recent advances in the design, formulation, and delivery of skin-mediated therapies and vaccines.

With Representation From:
Thursday, September 28, 2017

Complimentary Breakfast & Chairperson’s Welcome and Opening Remarks

**The Transdermal & Intradermal Landscape—Key Challenges and Opportunities**

8:15

How Challenges Evolve for Delivery into Skin as we Transition from Passive Diffusion to Delivery Technologies

Dr. Ajay Banga, Chair & Professor of Pharmaceutical Sciences, Mercer University

- Moderately lipophilic drugs can passively diffuse into skin but even these simple patches are considered to be drug-device combinations and face challenges such as drug crystallization, cold flow, or failure of adhesive. Hydrophilic molecules and macromolecules do not normally pass through the skin unless enabling technologies are used, and these offer different types of challenges. For example, iontophoresis is limited to deliver molecules up to around 13kDa and may potentially induce skin burns if skin contact is not uniform. Sonophoresis and laser-based devices may face challenges to miniaturize the device for home use by patients. Innovations and challenges in these technologies, especially for iontophoresis, ablative and non-ablative fractional laser, and microneedle-based devices, will be presented.

- Learn about challenges facing passive patch development, e.g., drug crystallization and how these challenges change as we move into delivery technologies, e.g., potential burns with an iontophoretic patch.
- Learn how new technologies are expanding the scope of transdermal delivery to include hydrophilic macromolecules.
- Learn the success and failures of novel skin delivery technologies developed and marketed over the years.

8:55

Keynote: Recent Advancements in Intradermal Delivery of Biopharmaceuticals

Lisa Dick, Ph.D., Lab Manager & Technology Leader, 3M Drug Delivery Systems

- As population demographics shift and new medicines become available, patient preferences and new technologies remain top of mind at 3M. In recent years, 3M has been developing a patient-friendly and easy-to-use microstructured transdermal system drug delivery platform that includes solid and hollow microneedle options along with associated applicators. These devices are well suited for dermal skin targets or systemic distribution for drugs that enter the lymphatic system. This talk will include recently generated data and examples that support intradermal delivery as a method to meet the evolving needs of pharmaceutical companies, regulators, providers, and patients.

9:35

Streamlined 505(b)(2) Transdermal Development Pathway for Potentially Faster Commercialization

Bobby Singh, Ph.D., Chief Technology Officer, Corium International

Abstract Coming Soon

10:15

Networking Coffee Break

10:40

Critical Issues—The Pharmacokinetics of Transdermal Delivery

Minimization of CYP2D6 Polymorphic Differences and Improved Bioavailability via Transdermal Administration

Thean Yeoh, Ph.D., Associate Research Fellow, Pfizer

- Transdermal delivery has the potential to offer improved bioavailability by circumventing first-pass gut and hepatic metabolism. This presentation will describe pharmacokinetic differences between transdermal and oral delivery of latrepirdine in extensive and poor CYP2D6 metabolizers (EM/PM). Dose-normalized latrepirdine total exposures were approximately 11-fold and 1.5-fold higher in EMs and PMs, respectively following administration of transdermal relative to oral. Differences between EM and PM latrepirdine exposures were decreased, with PMs having 1.9- and 2.7-fold higher peak and total exposures, respectively, following transdermal administration compared to 11- and 20-fold higher exposure, respectively, following oral administration. Transdermal delivery can potentially mitigate the large intersubject differences observed with compounds metabolized primarily by CYP2D6. Transdermal delivery was readily accomplished in this early clinic evaluation using an extemporaneously prepared solution.

11:20

Spotlight on Microneedle Arrays—The Present & (Near) Future of Microneedle Drug Delivery

How Microneedle Arrays Can Overcome the Challenges Facing Transdermal Drug Delivery

Dr. Ryan F. Donnelly, Chair in Pharmaceutical Technology, Queen’s University Belfast

- Transdermal delivery using conventional passive patches has perhaps passed its peak. Second generation physical enhancement techniques, such as ultrasound and iontophoresis have not progressed as once hoped. Research based upon microneedle arrays has intensified recently. While the initial focus was on biomolecules, the field has expanded to include delivery of conventional small molecule drugs. Much success has been achieved, particularly in the vaccines field. Recent innovations have focused on enhanced formulation design, allowing delivery of clinically relevant doses of small molecule...
drugs and biomolecules, larger patch sizes and scalable manufacture. However, no true microneedle-based drug delivery system has yet been marketed. A number of regulatory and manufacturability queries have been raised and those in the field are now actively working to address them. Microneedle-based transdermal drug delivery systems have tremendous potential to yield real benefits for patients and industry, especially if they can be shown to deliver therapeutic doses of drugs clinically, rather than simply vaccines. Through diligence, innovation and collaboration, this will begin to be realized over the next 3–5 years.

Complimentary Networking Lunch

Sponsored by

CSP TECHNOLOGIES

Your product, actively protected

Clinical Trial Experience with the Intracutaneous Microneedle Systems: Experience in Osteoporosis, Diabetes, and Migraine

Pete Schmidt, Senior Medical Director, Zosano Pharma

Zosano has developed intracutaneous microneedle systems for parathyroid hormone, glucagon, and zolmitriptan. Previously, we reported results from a 6-month study in post-menopausal females with osteoporosis, and reversal of insulin-induced hypoglycemia in Type 1 Diabetes Mellitus subjects. Most recently, we announced results of a 589-subject placebo-controlled trial in subjects with migraine. In that trial, intracutaneously administered zolmitriptan was highly effective for the treatment of migraine, with statistical significance compared to placebo achieved for the two co-primary endpoints of pain freedom at 2 hours, and most bothersome symptom absence at 2 hours. We believe this trial will form the basis for approval, in conjunction with an ongoing long term safety study. In addition to efficacy observed in this trial, tolerability was also good, as the most common adverse events were application site reactions of short duration. Nearly all subjects in the trial were able to use the applicator and patch on an outpatient basis to administer study drug. A non-oral route of administration is particularly valuable in migraine, where speed of onset is critical for producing relief, and gastric stasis is often present, which slows the absorption of orally-administered products. Our results in three different patient populations demonstrate the utility of the intracutaneous microneedle systems for delivering drugs rapidly and producing pharmacologic effects quickly. We intend to seek registration of the zolmitriptan system in less than two years and believe it will be an important addition to the products available to treat migraine. It will also demonstrate that this route of administration has great potential for the rapid delivery of a number of therapeutic compounds.

Sustained Delivery of an HIV Subunit Vaccine Using Silk Microneedle Skin Patches Promotes Robust Immune Responses

Dr. Archana V. Boopathy, Postdoctoral Researcher, Massachusetts Inst. of Technology (Contributing Authors: Anasuya Mandal, Dan W Kulp, Sudha Kumari, Wade Wang, Nitasha R Bennett, Yanpu He Talar Tokatlian, William R Schief, Paula T Hammond, and Darrell J Irvine)

Novel immunogen design and vaccine delivery strategies are critical for the development of an effective prophylactic HIV vaccine. Recent studies in our laboratories have shown that the kinetics of vaccine exposure modulate humoral immune responses. To control release kinetics in the setting of a prophylactic HIV vaccine, we developed a dissolving microneedle patch (MN) that implants a solid polymer tip carrying antigen and adjuvant into the skin, with release kinetics dependent on MN composition. We utilized silk protein to form MN tips encapsulating an HIV envelope trimer (SOSIP) and adjuvants, supported on a poly acrylic acid (PAA) base. Upon dermal application, rapid PAA dissolution is followed by sustained release of vaccine, with release kinetics regulated by the degree of beta-sheet crystallinity in the silk. Antigenicity of SOSIP encapsulated and subsequently released from silk was maintained, as determined by binding to broadly neutralizing antibodies (bNAb: PGT151, PGT145, PGT121 and VRC01) without binding to non-bNAb (39F, 14e, 4025 and B6). Following immunization in mice, we observed SOSIP and silk co-retention at the skin site of MN application over time. In the draining lymph nodes, MN delivery resulted in significantly higher SOSIP retention compared to intraderal injections. Further, silk MNs promoted germinal center (GC) responses in lymph nodes with significantly higher GC B cells and T follicular helper cells for at least 14 days following immunization compared to intraderal injections, and substantial increases in anti-SOSIP IgG titers. These results suggest the potential of silk MNs in modulating release kinetics of HIV subunit vaccine.

Thermostable Oxytocin-Coated Microneedle Patches

Dr. Yasmine Gomaa, Research Scientist, School of Chemical & Biomolecular Engineering, Georgia Tech (Contributing Authors: Chandana Kolluru, Mikolaj Milewski, Jingtao Zhang, Robert Saklatvala, Mark Prausnitz.)

Oxytocin (OX) is a nonapeptide hormone produced by the hypothalamus and secreted by the pituitary gland with both peripheral and central actions. Peripheral actions of OX have been known for years in promoting lactation, inducing delivery and preventing/treating postpartum hemorrhage. Central actions of oxytocin have recently attracted attention due to OX-mediated behavioral effects and its potential use in treatment of conditions such as schizophrenia and autism. OX is available as injections or nasal sprays with the need for a cold chain of storage.
Microneedles to Treat Pain of the Temporomandibular Disorders

Dr. Harvinder Gill, Associate Professor of Chemical Engineering, Texas Tech

Temporomandibular disorders (TMDs) include conditions characterized by pain and/or dysfunction in the temporomandibular joint (TMJ) and masticatory muscles. Pain control is a major objective in the management of TMDs and is the primary reason for patients to seek treatment. In the US, an estimated 5% to 12% of the population is affected by TMDs, and about 4 billion US dollars are spent annually to manage TMDs. Presently there is lack of both an effective pharmacological agent and a delivery method for the treatment of TMD-associated pain conditions. The compound, 15-deoxy-Δ12,14-prostaglandin J2 (15d-PGJ2) has anti-inflammatory properties and is naturally formed in the human body, and is thus safe. We have previously shown that an intra-TMJ injection of 15d-PGJ2 in nanogram amounts can alleviate TMJ pain in a rat model. However, intra-TMJ injections are painful. We next hypothesized that instead of injections, microneedles could be used for topical delivery of 15d-PGJ2. In this study we have evaluated microneedles for transdermal delivery of 15d-PGJ2 and compared it to the intra-TMJ injection in a rat model of TMJ pain. The results of this study will be discussed to show that microneedles can offer better and longer lived treatment response as compared to intra-TMJ injections.
The Advances in Bioequivalence Assessment of Generic Topical Drugs
Theo Kapanadze, Chief Scientific Officer, Diteba

In accordance with the recently released FDA draft guidance on acyclovir, Diteba presents on a fully compliant approach that combines the extensive acyclovir in vitro release testing (IVRT) and in vitro skin permeation testing (IVPT). This approach provides drug companies with the optimal chance of bio waiver success in lieu of the high cost and long delivery times associated with human clinical trials.

Critical Issues—Assessing TD and ID Absorption

Getting a Handle on Variability in Transdermal Absorption Assessment: In Silico, In Vitro, and In Vivo Methods
Mikolaj Milewski, Ph.D., Associate Principal Scientist, Merck

One of the key parameters to be evaluated as part of any transdermal drug delivery feasibility assessment is the maximum flux across the skin. There is no shortage of in silico, in vitro, and in vivo methods that address this question. Early stages of drug development usually employ simple in silico methods with limited inputs and provide a rough maximum skin absorption rate estimate. More time-consuming experimental in vitro diffusion studies can provide a better measure of the percutaneous flux at later stages. Finally, in vivo studies represent an ultimate test for a transdermal product. But is it really so?

Here we will examine the variability in the estimation of maximum percutaneous flux using different predictive methods as compared to the clinical absorption rates from approved marketed transdermal drug delivery systems. The analysis will highlight the performance of 1) selected predictive equations, 2) in vitro transdermal permeation from saturated drug solutions, and 3) in vitro transdermal permeation from prototype patches; as they compare to in vivo transdermal permeation from marketed patches. As a result an appreciation will be developed for varying degree of predictive power and cautious data interpretation.

Why Is Intradermal Absorption Faster than Subcutaneous?
Yash Kapoor, Ph.D., Associate Principal Scientist, Merck

Delivery through the skin remains an interesting area of research though the barrier properties of the skin limit the opportunities in this drug delivery platform. Passing the transdermal barrier to deliver drug inside the dermis, technologies such as microneedles, electroporation, etc. have been introduced and explored in the past few de-
ability to penetrate bacterial biofilms. Such ionic liquids can offer novel means to treat a variety of skin conditions of infectious origin. Second, ionic liquids can serve as designer solvents for topical delivery of hydrophilic, hydrophobic, charged and macromolecular drugs. Since the ionic liquids can be tuned by selecting various anions and cations, this approach provides excellent flexibility for designing solvents. In addition, we have also shown that by selecting the right counter ion, ionic liquids offer reduction of the dose-dependent toxicity of actives that otherwise cause skin irritation. I will present examples of these applications of ionic liquids, which collectively demonstrate that ionic liquids hold promise as a novel and unique platform for skin applications.

**Research Spotlight—Computational Modeling for Intradermal Delivery**

**Update on Computational Model for Dermal Transport and Clearance**

*Dr. Gerald B. Kasting, Professor of Pharmaceutics and Cosmetic Science, University of Cincinnati*

Unlike transdermal delivery, intradermal delivery is largely controlled by the physiology and transport properties of the lower skin layers. Clearance of an injected drug is governed by the interplay of hydrostatic and osmotic pressure, blood capillary density and permeability and lymphatic flow, as well as compound specific factors such as partitioning and protein binding. These factors vary between individuals and from site-to-site. We have developed a spreadsheet-based computational model for dermal clearance and transport that incorporates both the physiological and chemical-specific factors; thus can be used to guide the development of intradermal and (with appropriate modifications) subcutaneous injection technology. Example calculations involving specific macromolecules will be presented.

**Heat Effects and IVIVC in Transdermal and Topical Drug Delivery**

*Audra Stinchcomb, Ph.D., Chief Scientific Officer and Founder of F6 Pharma Inc.; Professor, University of Maryland*

An in vitro model that exhibits IVIVC is a powerful tool in biopharmaceutical drug development because it can efficiently predict drug product performance in vivo. While the concept of IVIVC has been utilized most often for oral dosage forms, demonstrations of IVIVC with in vitro models used for other dosage forms are emerging. The present investigation used multiple approaches to develop a Level A IVIVC for Transdermal Delivery Systems (TDS). Additionally, the effect of transient heat exposure on the rate and extent of TDS drug delivery was concurrently evaluated. Two model drug molecules, nicotine and fentanyl, with different physicochemical characteristics (e.g. log P) were evaluated in the current study. Early study results will also be reported for lidocaine and buprenorphine IVIVC.

**Advancements in Intradermal Drug Delivery**

*Glen Zimmermann, Director of Product Management, West Pharmaceutical Services*

Currently, IM and SC are the most common methods for delivery of non-infused drugs however, the skin contains a high concentration of antigen presenting cells, making it an ideal location for injection. These cells perform an essential role in processing incoming antigens, resulting in powerful immune system responses. Delivery of vaccines to the epidermis or dermis may result in superior immune responses when compared to IM or SC injections. In addition to the enhanced immune response in patients, ID delivery offers a variety of benefits to pharmaceutical manufacturers, including dose sparing, increased availability of limited or expensive antigens, and reduced cost per dose.

Typically ID injection is administered using the Mantoux technique, which requires special training and may not effectively target the skin resulting in delivery to the SC tissue (too deep) or leakage (too shallow). The difficulty associated with training and the inconsistency of injection efficacy have deterred medical practitioners from using ID injection as a common immunization method. In response to this, new devices have emerged to eliminate the challenges associated with performing an ID injection. This presentation will review some of the more recent advances in ID drug delivery systems.
Extractable and Leachable Testing for Transdermal Drug Delivery Systems: How to Resolve FDA Deficiency Situations Related to Those Issues

Gyorgy Vas, Ph.D., Trace Organic Analytical Group, Intertek Pharmaceutical Services (Contributing Authors: Louis Fleck, Howard Carpenter.)

Transdermal drug delivery systems are relatively complex pharmaceutical products. The formulation contains multiple excipients and in addition a dermal contact adhesive. The performance of the delivery systems depends on the quality of the dermal adhesive and the formulation, which delivers the drug on a pre-determined rate. The dermal delivery route is getting more and more popular, since the effect of the delivered drug can be localized, which may reduce the systemic side effects. However since the formulation has extended contact time, besides the drug is being delivered excipients, degradation products and packaging related components can also be “delivered” with the same route of administration. The extractable testing of transdermal systems are straightforward, does not requires “out of box” thinking. The leachables testing requires more complex approaches, as the regulatory expectation is to test the finished products with biologically relevant extraction media.

The presentation will focus on different test approaches, to present options for leachable testing, how to evaluate the actual leachables and validate analytical methods what are requires non-routine extraction methods and as well detection capability down to ppb level. The complex formulation combined with the low level testing requirement are very challenging analytical task. Component identification, analytical method development and validation are not as simple as for the components present at a ppm level or above. The presentation will also presenting case studies and solutions for non-conformance situations related to TDS systems.

Critical Issues—IVPT & IVRT of Transdermal and Topical Products

Evolution of the in vitro Permeation (IVPT) and in vitro Release (IVRT) Tests—Coming of Age

Paul Lehman, VP and Head of Dermal & Transdermal Research Services, QPS Holdings, LLC

Since the innovation of the Franz Diffusion Cell and the Finite Dose Model by Dr. Thomas Franz, c1974, their simple and elegant value has matured over the years to become a more complex contribution to the advancement of semi-solid and transdermal delivery systems to the industry. Today, the use of the diffusion cell is at the threshold of being fully recognized as a surrogate model for the determination of bioequivalence for topical semi-solid formulations. However, the complete passage into full acceptance and recognition requires the same scrutiny that any other surrogate model requires, namely validation, whether for IVPT or IVRT. Validation requires the demonstration of procedural standardization, sensitivity, selectivity, reproducibility and robustness. These factors will be discussed, and as to whether they actually do contribute to substantiating the validity of the models.

Close of Program
About your conference destination:
The Racquet Club of Philadelphia is located in the heart of downtown Philadelphia, adjacent to beautiful Rittenhouse Square. From the conference venue, you can access many points of interest in Philadelphia including Independence Hall, the Kimmel Center, the Avenue of the Arts, numerous shops, and excellent restaurants!

Register Information

Register for the conference using one of three options:
Online: www.pharmaedresources.com  Phone: (217) 721-5774
Mail: 2810 Robeson Park Drive, Champaign, IL 61822

Please Complete the Following
FIRST NAME: ___________________________
LAST NAME: ___________________________
TITLE: ________________________________
COMPANY: ____________________________
ADDRESS: _____________________________
ADDRESS: _____________________________
CITY: _______ STATE: _________________
ZIP: _______ COUNTRY CODE: __________
OFFICE PHONE: _______________________
MOBILE PHONE: _______________________
FAX: _________________________________
E-MAIL: ______________________________

Please register me for:
Transdermal & Intradermal Drug Delivery Systems 2017: Advanced Design, Development & Delivery of Skin-Mediated Therapies and Vaccines

Standard Registration: $1,595
Spring Special: Register before May 15th & take $300 off!
Early Bird: Register by July 15th & take $200 off!
Call for government or academic discount

PAYMENT METHOD
CREDIT CARD REGISTRATION:
☐ CREDIT CARD  ☐ VISA  ☐ MASTERCARD  ☐ AMEX
NAME: _______________________________
CARD #: ______________________________
EXPIRATION: _____ / _____
SIGNATURE: _________________________
BILLING ADDRESS: ___________________

CHECK REGISTRATION:
To pay by check, please provide a purchase order below. Please note that all payments must be received five (5) days prior to the conference to ensure space. Attendees will not be admitted to the conference without full payment.
PURCHASE ORDER #:

PLEASE NOTE:
PharmaEd Resources does not offer refunds. However, if you cannot attend after registering, we are happy to apply your registration fee to another PharmaEd Resources event, or transfer your registration to a colleague. Notice of cancellation must be received at least 5 days prior to the event.