DTSS RECEPTION

Dermal Toxicology Specialty Section
Virtual Reception
March 17, 5-6 pm, 2021
Current Officers

President
Neera Tewari-Singh, MS, PhD

Vice President
Sara Farahmand, PhD

Vice President-Elect
Vacant

Secretary/Treasurer
Yoke-Chen Chang, PhD

Past President
Michael Hughes, PhD, DABT

Senior Councilor
Jeffrey Moehlenkamp, PhD, DABT

Councilor
Gabriel Knudsen, PhD, DABT
Current Representatives

• Postdoctoral Representative
  • Ana Ferragut Cardoso, PhD

• Graduate Student Representative
  • Careen Khachatoorian, PhD
Thank You to DTSS Officers Rotating off the Committee!

Michael Hughes
Jeffrey Moehlenkamp
Congratulations to New DTSS Officers!

• Vice President
  • Sam Tadepalli
• Councilor
  • Michael D. Southall

We need a volunteer for our Vice-President Elect position
Thanks to All Our Sponsors

Michael Hughes for Student support
DTSS Activities 2020-2021

• Sponsored workshop at 2021 Annual Virtual Meeting

  Applicability Domains and Future of Nonanimal Tests for Skin Sensitization” Wednesday, March 24th (11:45 am – 2:30 pm)
  Chair(s): Victor J. Johnson, Burleson Research Technologies; and Marc Pallardy, Université Paris-Sud, France
DTSS Activities 2020-2021

• Initiated Program to Sponsor Graduate Student Memberships
• Posted DTSS Officer Roles and Responsibilities on DTSS website
• Published DTSS Newsletter
• DTSS poster prepared for Annual Meeting
• Reviewed several proposals and papers for DTSS awards
Skin and Dermal Toxicity Session

Poster Session:

Skin and Dermal Toxicity
Chair(s): Jeffrey Yourick, US FDA
Tuesday, March 23rd (1-2:45pm)
Secretary/Treasurer’s Report
Secretary/Treasurer’s Report

• As of March 1, 2021, DTSS currently has 128 members (8 students, 3 post-doctoral fellows).

• At the end of 2020, DTSS had cash reserves of $8,704 Compared to $3,880 at the end of 2019 
  Current reserve is sufficient to cover the annual reception and student awards

• We encourage members to consider contributing to DTSS 
  Send contributions to SOT, c/o Belinda Inscho and specifically note DTSS
Special Program to Recruit Graduate Student Members

• The DTSS is offering a membership program to 6 graduate students for free membership to the specialty section

• If you have a lab colleague who might be interested in becoming a DTSS graduate student member, encourage them to contact Bo Inscho at SOT headquarters
Session proposals for SOT 2022

- Symposia
- Workshops
- Roundtable
- Informational Session
- Continuing Education

Contact for more information or send proposals to Sara Farahmand at farahmand.s@gmail.com or Neera Tewari Singh at tewarsi@msu.edu for feedback from DTSS

Please send proposals two-three weeks before the final deadline for SOT proposal submissions which might be late April or early May.
Award Presentations

• Informa Healthcare Award
• DTSS Paper of The Year Award
• Stratacor Postdoctoral Award
• DTSS Postdoctoral Award sponsored by Charles River
• DTSS Student Award sponsored by Charles River
Informa Healthcare Award

In recognition of the best paper in dermal toxicology published in Cutaneous and Ocular Toxicology

Anti-inflammatory effect of Arnica montana in a UVB radiation-induced skin-burn model in mice


Cutaneous and Ocular Toxicology, 2020 Jun;39(2):126-133.
Paper of The Year Award

In Recognition of an Exceptional Publication in the Field of Skin Toxicology and Pharmacology

Nancy Hopf, PhD., et al.
University of Lausanne

“Reflections on the OECD guidelines for in vitro skin absorption studies”
Stratacor Postdoctoral Award

In Recognition of Outstanding Postdoctoral Candidates for their Contribution to Skin-related Research

Satyendra Singh, PhD
Michigan State University

“Mechanism mediating the Dermal Inflammation and Toxicity from Phosgene Oxime Exposure”
DTSS Student Award Sponsored by Charles River

In Recognition of an Outstanding Graduate Student for Skin-related Research

Careen Khachatoorian
University of California, Riverside

"Electronic cigarette fluids and exhaled residue cause an inflammatory response in both human keratinocytes and a 3D skin model"
DTSS Postdoctoral Fellow Award Sponsored by Charles River

In recognition of outstanding postdoctoral fellow for their contribution to skin-related research

Swati Sharma, Ph.D.
Michigan State University

“Mechanisms contributing to skin inflammatory pathology following exposure to Environmental pollutant Benzo(a) Pyrene in Psoriatic mouse model”
Award Winners 2020

**Informa Healthcare Award**

**DTSS Paper of the Year Award**

**Stratacor Postdoctoral Award**
- Ana Cardoso, PhD (University of Louisville). Alternative Splicing as a Key Mechanism in Arsenic-Induced Squamous Cell Carcinoma: Evidence from RNA-Seq and Proteomic Analysis.
Award Winners 2020

Student Research Award

• **Bryan Holloman (University of South Carolina, School of Medicine).** Role of Aryl Hydrocarbon Receptor ligands in allograft rejection.

Charles River Student and Postdoctoral Fellow Travel Awards

• **Satyendra Singh, PhD (Michigan State University).** Toxicologic pathology and related mechanism following cutaneous exposure of phosgene oxime.

• **Rachel Baur (West Virginia University).** Alterations in the Mouse Skin and Gut Microbiome and Skin Integrity Following Dermal Exposure to the Antimicrobial Chemical Triclosan
Reflections on the OECD guidelines for
*in vitro* skin absorption studies

N.B. Hopf\textsuperscript{a}, C. Champmartin\textsuperscript{c}, L. Schenk\textsuperscript{b}, A. Berthet\textsuperscript{a}, L. Chedik\textsuperscript{c}, J.L. Du Plessis\textsuperscript{j}, A. Franken\textsuperscript{i}, F. Frasch, S. Gaskin\textsuperscript{a}, G. Johanson\textsuperscript{b}, A. Julander\textsuperscript{b}, G. Kasting\textsuperscript{h}, S. Kilo\textsuperscript{d}, F. Larese Filon\textsuperscript{f}, F. Marquet\textsuperscript{c}, K. Midander\textsuperscript{b}, E. Reale\textsuperscript{a}, A.L. Bunge\textsuperscript{g}

\textsuperscript{a} Centre for Primary Care and Public Health (Unisante), Department for Occupational and Environmental Health (DSTE), Exposure Science Unit, Switzerland
\textsuperscript{b} Karolinska Institutet, Institute of Environmental Medicine, Unit of Integrative Toxicology, Sweden
\textsuperscript{c} French National Research and Safety Institute for the Prevention of Occupational Accidents and Diseases (INRS), France
\textsuperscript{d} Friedrich-Alexander University Erlangen-Nürnberg, Institute and Outpatient Clinic of Occupational, Social and Environmental Medicine, Germany
\textsuperscript{e} University of Adelaide, School of Public Health, Health and Medical Sciences, Australia
\textsuperscript{f} University of Trieste, Clinical Unit of Occupational Medicine, Department of Medical, Surgical and Health Sciences, Italy
\textsuperscript{g} Colorado School of Mines, Chemical and Biological Engineering, USA
\textsuperscript{h} University of Cincinnati, James L. Winkle College of Pharmacy, USA
\textsuperscript{i} Occupational Hygiene and Health Research Initiative (OHHRI) North-West University, South Africa
Background

Method

Substance/solution tested

Skin

Sampling at different time points for a defined period of time

Drawing by permegear.com

Quantification of the substance/metabolite

Results

Cumulative amount per area (µg/cm²)

Slope = J

Absorption/permeation rate (J)
Mass of test substance passing through a unit area of skin into the receptor fluid or systemic circulation, per unit time (µg/cm²/h)

Steady-state
the part of an absorption profile where the absorption rate remains constant

Lag time ($T_{lag}$)
derived from a graph of cumulative absorbed dose and time (h)

Permeability coefficient: $Kp \ [cm/h] = \frac{J_{steady-state}}{(applied \ conc. \ [µg/cm^3])}$

$Kp$ represents the rate at which a chemical penetrates the skin

https://permegear.com/franz-cells/
Goals

Aims:
1) assist other skin absorption laboratories in planning their experiments considering factors that are currently not defined in the OECD documents; and
2) provide some practical insights to the OECD expert group that currently is revising the GN156-2019 guideline.

The overall goal is to contribute to the harmonization of skin permeation experiments and standardization of reported outputs

The paper discusses many OECD guidance themes:
• Terminology and scope
• Experimental equipment (diffusion cell, receptor fluid, sampling, temperature)
• Skin (skin procurement and preparation, skin thickness, skin integrity, skin viability)
• Substance application (test substance concentrations and formulations, application to the skin, recovery procedures, chemical analysis,)
• Statistics (data, replicates, and test report)
• Interpretation of in vitro data
Ex. Terminology

- penetration, permeation, absorption

**Penetration** - entry of a substance into the stratum corneum and permeation through epidermis.

**Permeation**

**Absorption** - a process that describes the passage of compounds across the skin and includes penetration.
Recommendations

One overarching recommendation

- The GN156 should be revised to clearly address all types of chemicals tested for skin permeation (individual chemicals, formulations, pesticides, biocides, powders, mixtures)
- The GN156 revision should be followed by revisions of the GD28 and TGD428; as all three documents need to be updated and harmonized.

Specifically,

- Use the same terminology in all guidelines
- Add a section on theoretical basis of the skin permeation parameters and possible limitations in using these in risk assessment
- Add examples of appropriate vehicles and receptor fluid for poorly soluble analytes
- Provide examples of reliable methods for assessing skin viability and integrity, including criteria for acceptable integrity
- Include protocols describing how to conduct mass-balance, tape strip methods, and skin extractions.
Mechanism Mediating the Dermal Inflammation and Toxicity from Phosgene Oxime Exposure

Satyendra K Singh¹, Dinesh G Goswami²,⁴, Claire R Crouchtch³, Rajesh Agarwal⁴, Erica L Noland⁵, Neera Tewari-Singh¹

¹. Department of Pharmacology and Toxicology, Michigan State University, East Lansing, MI; 2. Department of Molecular and Translational Medicine, Texas Tech University Health Sciences Center, El Paso, TX; 3. MRIGlobal, Kansas City, MO; 4. Department of Pharmaceutical Sciences, University of Colorado Denver, Aurora, CO; 5. Department of Pathobiology and Diagnostic Investigation, Michigan State University, East Lansing, MI
Introduction

- Phosgene oxime (CX), a halogenated oxime, is an urticant or nettle agent with highly volatile, reactive, corrosive, and irritating vapor.

- CX is absorbed quickly through the clothing with faster cutaneous penetration compared to other vesicating agents causing instantaneous pain and severe tissue damage, and death.

- The skin urticaria from CX resembles urticaria caused by allergic and non-allergic reactions to various environmental substances.

<table>
<thead>
<tr>
<th>Chemical Agent</th>
<th>Pain</th>
<th>Tissue Damage</th>
<th>Blister</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sulfur Mustard</td>
<td>Hours later</td>
<td>Onset of clinical effects is hours (24h)</td>
<td>Fluid filled</td>
</tr>
<tr>
<td>Lewisite</td>
<td>Immediate</td>
<td>Seconds to minutes</td>
<td>Fluid filled</td>
</tr>
<tr>
<td>Phosgene Oxime</td>
<td>Immediate</td>
<td>Seconds</td>
<td>Solid wheal</td>
</tr>
</tbody>
</table>
Introduction

• It is one of the least studied warfare agent with no specific antidote available.

• Information on its dermal absorption and effects on human skin tissue is limited, and its mechanism of action is unknown.

• Our studies are focused on developing a well-defined mouse toxicity model of CX-skin exposure and a mechanistic base which could be employed for the identification of novel targets that could be explored for therapeutic intervention.

• Our current studies could have a profound impact on understanding the toxic effects, pathology and related molecular mechanism of CX cutaneous toxicity with significant translational implications towards designing intervention strategies.
CX Exposure-Duration and Time-Response Study Paradigm

SKH-1 hairless mouse

Topical exposure to 10 μl CX vapor using two 12 mm vapor caps, one at each side of dorsal skin of mice

Clinical assessments and observations

0h 0.5h* 2h* 8h* 1 day

CX 1min exposure

0h 2h* 1 day* 3 day 7 day 14 day*

CX 0.5min exposure

*, time points at which mice were euthanized and skin tissues were collected for histopathological and molecular analyses
CX skin exposure increased epidermal cell death

TUNEL assay

1 min CX Exposure

Male

Control

30 mins

2 hours

8 hours

0.5 min CX Exposure

Male

Control

2 hours

24 hours

14 days

Female

Control

2 hours

24 hours

14 days

e, epidermis; d, dermis; ***, P<0.001; ****, P<0.0001
CX skin exposure increased oxidative DNA damage

8-OHdG staining

1 min CX Exposure

0.5 min CX Exposure

Control

30 mins

2 hours

8 hours

Male

16.7 μm

50 μm

Control

2 hours

24 hours

14 days

Male

16.7 μm

50 μm

Control

2 hours

24 hours

14 days

Female

16.7 μm

50 μm

e, epidermis; d, dermis; *, P<0.05; **, P<0.01
CX skin exposure increased expression of DNA damage markers

**DNA damage markers**

**1 min CX exposure**

<table>
<thead>
<tr>
<th>Male mice</th>
<th>Control</th>
<th>30 mins</th>
<th>2 hours</th>
<th>8 hours</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>pP53</td>
<td>P53</td>
<td>β-Actin</td>
<td>γH2A.X</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

**0.5 min CX exposure**

<table>
<thead>
<tr>
<th>Male mice</th>
<th>Control</th>
<th>2 hours</th>
<th>24 hours</th>
<th>14 days</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>pP53</td>
<td>P53</td>
<td>β-Actin</td>
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<td></td>
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<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Female mice</th>
<th>Control</th>
<th>2 hours</th>
<th>24 hours</th>
<th>14 days</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>pP53</td>
<td>P53</td>
<td>β-Actin</td>
<td>γH2A.X</td>
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<tr>
<td></td>
<td></td>
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<td></td>
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</tr>
</tbody>
</table>
CX skin exposure increased oxidative stress marker

1 min CX exposure

Control 30 mins 2 hours 8 hours

Male mice

HO-1  β-Actin

0.5 min CX exposure

Control 2 hours 24 hours 14 days

Male mice

HO-1  β-Actin

Female mice

HO-1  β-Actin

HO-1, Heme Oxygenase-1
CX skin exposure increased mast cell and neutrophils activation.
CX skin exposure increased expression of DNA damage and inflammatory markers

### Inflammatory markers

#### 1 min CX exposure

- Control
- 30 mins
- 2 hours
- 8 hours

- COX2
- β-Actin
- MMP9
- β-Actin
- pJNK 1/2
- JNK 1/2
- β-Actin

#### 0.5 min CX exposure

- Control
- 2 hours
- 24 hours
- 14 days

- COX2
- β-Actin
- MMP9
- β-Actin
- pJNK 1/2
- JNK 1/2
- β-Actin

- Control
- 2 hours
- 24 hours
- 14 days

- COX2
- β-Actin
- MMP9
- β-Actin
- pJNK 1/2
- JNK 1/2
- β-Actin
CX skin exposure increased Activator Protein-1

1 min CX exposure

Control 30 mins 2 hours 8 hours

p-cJun
cJun
TBP

0.5 min CX exposure

Control 2 hours 24 hours 14 days

p-cJun
cJun
TBP

Control 2 hours 24 hours 14 days

p-cJun
cJun
TBP
CX skin exposure increased inflammatory cytokine

<table>
<thead>
<tr>
<th>Cytokines</th>
<th>1 min CX exposure</th>
<th>0.5 min CX exposure</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Male mice (fold change)</td>
<td>Male mice (fold change)</td>
</tr>
<tr>
<td></td>
<td>C vs. 30m</td>
<td>C vs. 2h</td>
</tr>
<tr>
<td>IL1</td>
<td>1.71</td>
<td>0.94</td>
</tr>
<tr>
<td>IL6</td>
<td>0.25</td>
<td>3.80</td>
</tr>
<tr>
<td>CXCL11</td>
<td>0.53</td>
<td>4.20</td>
</tr>
<tr>
<td>VEGF</td>
<td>0.80</td>
<td>1.08</td>
</tr>
<tr>
<td>IL4</td>
<td>0.03</td>
<td>0.15</td>
</tr>
<tr>
<td>IL10</td>
<td>0.00</td>
<td>0.05</td>
</tr>
</tbody>
</table>
CX skin exposures in SKH-1 hairless mice causes:
• Immediate skin lesions including urticaria, necrosis, blanching, erythema and edema, and mortality in long-duration exposed mice
• An increase in the skin epidermal and dermal plus hypodermal thickness
• Increases in the scab formation and hyperkeratosis
• Alterations of inflammatory, DNA damage and oxidative stress markers
• Alteration of inflammatory cytokine response
• An increase in skin mast cell activation
• These effects could be due to the activation of pathways related to mast cell activation, inflammation, and DNA damage
Funding

- Countermeasures Against Chemical Threats (CounterACT) Program, Office of the Director National Institutes of Health (NIH OD) and National Institute of Arthritis and Musculoskeletal and Skin Diseases (NIAMS) [Grant Numbers R21 AR073544 and U01 AR075470].
E-CIGARETTE FLUIDS AND EXHALED RESIDUE CAUSE AN INFLAMMATORY RESPONSE IN BOTH HUMAN KERATINOCYTES AND A 3D SKIN MODEL

Careen Khachatoorian
University of California, Riverside
DTSS Reception
March 17, 2021
ECEAR
ELECTRONIC CIGARETTE EXHALED AEROSOL RESIDUE

Nicotine + Flavor Chemicals
ECEAR EXPOSURE ROUTE

Epidermis

The Skin

- Dermal papilla
- Hair
- Sensory nerve ending
- Sebaceous gland
- Epidermis
- Dermis
- Subcutaneous layer
- Nerve
- Fat, collagen, fibroblasts
- Capillaries
- Arteriole
- Sweat glands
DEWBERRY CREAM AND CHURRIOS
REFILL FLUID CHEMICAL ANALYSIS

**A. Dewberry Cream**

- Guaiacol (2-methoxyphenol)
- Ethyl maltol
- Benzaldehyde
- Maltol
- Benzyl alcohol
- 2,3-Butanedione
- Vanillin
- Ethyl vanillin
- Benzyl benzoate
- Furaneol
- Hexyl acetate
- p-Anisaldehyde
- Isosafroleugenol
- Amyl acetate
- Isobuty1 acetate
- Ethyl 2-methylbutanoate
- Hemineurine
- Benzyl acetate
- Methyl cinnamate
- Linalool
- 2,3-Pentanedione
- Benzaldehyde PG acetal
- Ethyl propanoate
- δ-Decalactone
- γ-Octalactone
- (3Z)-3-Hexen-1-ol
- Acetoin
- γ-Decalactone
- α-Decalactone
- Ethyl hexanoate
- Butyl butyrolactate
- Isoamyl isovalerate
- Ethyl acetate
- γ-Nonalactone
- Ethyl lactate
- Ethyl butanoate
- Isoamyl acetate
- α-Unsdecalactone
- Hydroxyacetone
- Carylone
- 3-Hexen-1-ol, acetate, (Z)-
- Amyl isovalerate
- Nicotine

**B. Churrios**

- Coumarin
- Guaiacol (2-methoxyphenol)
- Ethyl maltol
- Maltol
- Benzyl alcohol
- Vanillin
- Ethyl vanillin
- Benzyl benzoate
- Cinnamaldehyde, (E)-
- p-Anisaldehyde
- Hemineurine
- Piperonal
- Ethyl propanoate
- γ-Octalactone
- Acetoin
- Isopentyl phenylacetate
- γ-Decalactone
- α-Decalactone
- Butyl butyrolactate
- Isoamyl isovalerate
- Ethyl acetate
- γ-Nonalactone
- Ethyl lactate
- Ethyl butanoate
- Carylone
- Triacetin
- Amyl isovalerate
- Nicotine

**Concentrations (mg/mL):**

- Dewberry Cream: 30, 10, 1, 0.1, 0.01
- Churrios: 19, 10, 1, 0.1, 0.01
Human Keratinocytes
CCD 1106 KERT\textsuperscript{r}
(ATCC® CRL-2309™)
**REACTIVE OXYGEN SPECIES**

- **ROS-Glo™** was used for H$_2$O$_2$ measurement.
- Upon addition of ROS-Glo™ Detection Reagent the luciferin reacts with Luciferase to generate a luminescent signal that is proportional to H$_2$O$_2$ concentration.
- **CellROX®** Green for detection of oxidative stress in live cells.
- **CellROX®** Green Reagent is a DNA dye, and upon oxidation, it binds to DNA; thus, its signal is localized primarily in the nucleus and mitochondria.
MATTEK EPIDERM™

- *In vitro* model system for chemical, pharmaceutical and skin care product testing to replace rabbit skin *in vivo* experiments
- Exposure is done at the air liquid interface
- The *In Vitro* EpiDerm™ Skin Irritation Test was followed to determine irritation
- Tissue and culture medium can be assayed.
EPIDERM™ EXPOSED TO REFILL FLUIDS

Dewberry Cream MTT

Churrios MTT

% of Control

4 hrs. 24 hrs.

10% 30% 100%

Dewberry Cream

Churrios

Positive CN

Negative CN

Dewberry Cream

Churrios
EPIDERM™ EXPOSED TO LAB MADE REFILL FLUIDS
ECEAR treatments did not produce effects in the MTT or LDH assay when Dewberry Cream was used to create ECEAR.

Similar results were obtained with ECEAR made from Churrios, except that there was a small (10%) (non-significant) increase in LDH activity in EpiDerm™ samples treated with ECEAR extracts for 24 hours.

IL-1α secretion was increased in both Dewberry Cream and Churrios ECEAR extract samples treated for 4 and 24 hours, but significance was observed only in the 24-hour Churrios extract.
• Keratinocytes were exposed to refill fluids to determine cytotoxicity.
  • Churrios was more cytotoxic than Dewberry Cream at 1% concentration and both fluids induced ROS production.

• 3D skin tissues were exposed to refill fluids and lab made fluids.
  • Refill fluids and all lab made refill fluids increased inflammatory markers upon exposure.
  • Inflammation was caused by PG, which is found in all E-liquid products.

• Exposure due to leakage or spills can increase oxidative stress and release of inflammatory proteins.

• The accumulation of ECEAR contributed to inflammation in 3D skin tissues.

• Longer and increased exposures should be done to understand a full range of responses to ECEAR.
ACKNOWLEDGMENTS

- Dr. Prue Talbot
- Talbot Lab
- Dr. Jim Pankow, Dr. Wentai Luo, Kevin McWhirter
- Tammy Nguyen

**Funding**

- TRDRP Grant #26IR-0018
- TRDRP Thirdhand Smoke Consortium #20PT-0184
- Armenian Engineers and Scientists of America Scholarship

- SOT Dermal Tox Specialty Section
Mechanisms Contributing to Skin Inflammatory Pathology Following Exposure to Environmental Pollutant Benzo(a) Pyrene in Psoriatic Mouse Model

Swati Sharma¹, Joshua A Klein¹, Satyendra K Singh¹, Dinesh G Goswami², Leah N Braucher¹, Holly N Wright¹, Erica L Noland¹; Rajesh Agarwal³; Neera Tewari-Singh¹

1. Michigan State University, East Lansing, MI; 2. Texas Tech University Health Sciences Center, El Paso, TX; and 3. University of Colorado³ Denver, Aurora, CO
Environmental chemicals like polycyclic aromatic hydrocarbons (PAHs) are a major concern as it could contribute to the pathophysiology of several chronic inflammatory skin diseases like atopic dermatitis and psoriasis.

Benzo[a]pyrene (BaP), the main source of atmospheric PAH, and is generated mainly from cigarette smoke, wood-burning and automobile exhaust.

BaP is known as one of the aggravating factor in inflammatory skin diseases which is characterize by neutrophil infiltration and induction of other proinflammatory cyto/chemokines.

The toxicity of PAHs is known to affect a variety of organs and cells via the aryl hydrocarbon receptor (AhR).

Information on its dermal absorption and effects on human skin tissue is limited, and its mechanism of action is unknown.
Study Design

**Study Design 1: (BAP+IMQ)**

62.5mg IMQ and 64 µg BaP in 50 µL acetone topically once daily alone or in combination.

Dorsal surface of mice shaved 2 days before exposure.

Day 1 2 3 4 5  Day 6
(BaP+IMQ)
Clinical assessments

Mice sacrificed and the skin tissue was collected for analysis.

**Study Design 2: BAP+IMQ**

64 µg BaP in 50µL acetone once daily for 5 days followed by 62.5mg IMQ once daily for 5 days.

Dorsal surface of mice shaved 2 days before exposure.

Day 1 2 3 4 5 6 7 8 9 10  Day 11

BaP IMQ
Clinical assessments

Mice sacrificed and the skin tissue was collected for analysis.
Effect of BaP Exposure on IMQ-induced psoriatic skin inflammation in C57BL/6 mice

Control | IMQ | Male Mice BaP | (BaP+IMQ) | BaP+IMQ
---|---|---|---|---
Edema, necrosis & scaly patches | Enhanced Edema, erythema | Necrosis, and scaly patches

Control | IMQ | Female Mice BaP | (BaP+IMQ) | BaP+IMQ
---|---|---|---|---
Edema, necrosis & scaly patches | Enhanced Edema, erythema | Necrosis, and scaly patches
Effect of BaP on IMQ-Induced Histopathological changes

Representative pictures showing histopathological changes in male C57BL/6 mice (10X magnification), rr, elongated rete ridges; a, acanthosis; di, dermal infiltrates; p, parakeratosis; ma, micro abscess; e, epidermis; d, dermis; h, hypodermis.
Effect of BaP on IMQ-Induced Epidermal Thickness

**Male**

Control vs IMQ: *P<0.05; **, P<0.01;***, P<0.0005; ****, P<0.0001 compared to control; ##, P<0.01; ###, P<0.0005 compared to IMQ

**Female**

Control vs IMQ: *P<0.05; **, P<0.01;***, P<0.0005; ****, P<0.0001 compared to control; ##, P<0.01; ###, P<0.0005 compared to IMQ
Effect of BaP on IMQ-Induced Dermal Thickness

***, P<0.001; ****, P<0.0001 compared to control; ##, P<0.01; ###, P<0.0005 compared to IMQ
Effect of BaP Exposure on IMQ-Induced Skin Leucocyte Accumulation

*, p<0.05 compared to control; #, p<0.05 compared to IMQ
Effect of BaP Exposure on the Expression of Inflammatory Markers
Summary

➢ Exposure of BaP causes an increase in inflammation in mice and aggravates IMQ-induced histopathological changes.

➢ BaP exposure enhances skin edema, necrosis, and dermal and epidermal thickness in both male and female groups of psoriatic mouse model.

➢ Protein expression of inflammatory markers like COX-2 and MMP9 and myeloperoxidase(MPO) was elevated in both male and female of BaP exposed psoriatic mouse model.

➢ Further mechanistic studies and metabolomics analysis in the skin tissue is being carried out to determine the changes in metabolites and identify the pathways involved.
Conclusion

➢ Present study reveals that exposure of BaP in IMQ-induced Psoriatic mouse model could activate inflammatory pathways by elevating the expression of inflammatory markers and further elevate the skin inflammation.

➢ Further mechanistic studies are needed to evaluate the pathways involved in BaP-induced exacerbation of psoriasis.
Acknowledgements

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Closing Remarks

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