

# Bulletin Board

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## CHEMICAL EFFECTS

## Transdermal permeation of inorganic cerium salts in intact human skin

2022-05-10

The stratum corneum protects the body against external agents, such as metals, chemicals, and toxics. Although it is considered poorly permeable to them, comprising the major barrier to the permeation of such substances, it may become a relevant gate of entry for such molecules. Cerium (Ce) is a lanthanide that is widely used in catalytic, energy, biological and medicinal applications, owing to its intrinsic structural and unique redox properties. Cerium salts used to produce cerium oxide (CeO<sub>2</sub>) nanostructures can potentially come into contact with the skin and be absorbed following dermal exposure. The objective of this study was to investigate the percutaneous absorption of three inorganic Ce salts: cerium (III) chloride (CeCl<sub>3</sub>); cerium (III) nitrate (Ce(NO<sub>3</sub>)<sub>3</sub>) and ammonium cerium (IV) nitrate (Ce(NH<sub>4</sub>)<sub>2</sub>(NO<sub>3</sub>)<sub>6</sub>), which are commonly adopted for the synthesis of CeO<sub>2</sub> using in vitro - ex vivo technique in Franz diffusion cells. The present work shows that Ce salts cannot permeate intact human skin, but they can penetrate significantly in the epidermis (up to 0.29 µg/cm<sup>2</sup>) and, to a lesser extent in dermis (up to 0.11 µg/cm<sup>2</sup>). Further studies are required to evaluate the potential effects of long-term exposure to Ce.

Authors: Greta Camilla Magnano, Giovanna Marussi, Francesca Larese Filon, Matteo Crosera, Massimo Bovenzi, Gianpiero Adami

Full Source: Toxicology in vitro : an international journal published in association with BIBRA 2022 May 10;82:105381. doi: 10.1016/j.tiv.2022.105381.

The stratum corneum protects the body against external agents, such as metals, chemicals, and toxics.

## On the Utility of ToxCast-Based Predictive Models to Evaluate Potential Metabolic Disruption by Environmental Chemicals

2022-05

Background: Research suggests environmental contaminants can impact metabolic health; however, high costs prohibit in vivo screening of putative metabolic disruptors. High-throughput screening programs, such as ToxCast, hold promise to reduce testing gaps and prioritize higher-order (in vivo) testing. Objectives: We sought to a) examine the concordance of in vitro testing in 3T3-L1 cells to a targeted literature review for 38 semivolatile environmental chemicals, and b) assess the predictive utility of various expert models using

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ToxCast data against the set of 38 reference chemicals. Methods: Using a set of 38 chemicals with previously published results in 3T3-L1 cells, we performed a metabolism-targeted literature review to determine consensus activity determinations. To assess ToxCast predictive utility, we used two published ToxPi models: a) the 8-Slice model published by Janesick et al. (2016) and b) the 5-Slice model published by Auerbach et al. (2016). We examined the performance of the two models against the Janesick in vitro results and our own 38-chemical reference set. We further evaluated the predictive performance of various modifications to these models using cytotoxicity filtering approaches and validated our best-performing model with new chemical testing in 3T3-L1 cells.

Results: The literature review revealed relevant publications for 30 out of the 38 chemicals (the remaining 8 chemicals were only examined in our previous 3T3-L1 testing). We observed a balanced accuracy (average of sensitivity and specificity) of 0.86 comparing our previous in vitro results to the literature-derived calls. ToxPi models provided balanced accuracies ranging from 0.55 to 0.88, depending on the model specifications and reference set. Validation chemical testing correctly predicted 29 of 30 chemicals as per 3T3-L1 testing, suggesting good adipogenic prediction performance for our best adapted model.

Discussion: Using the most recent ToxCast data and an updated ToxPi model, we found ToxCast performed similarly to that of our own 3T3-L1 testing in predicting consensus calls. Furthermore, we provide the full ranked list of largely untested chemicals with ToxPi scores that predict adipogenic activity and that require further investigation. <https://doi.org/10.1289/EHP6779>.

Authors: Dayne L Filer, Kate Hoffman, Robert M Sargis, Leonardo Trasande, Christopher D Kassotis

Full Source: Environmental health perspectives 2022 May;130(5):57005. doi: 10.1289/EHP6779.

Endometriosis is a disease characterized by the presence of the uterine endometrium outside of its normal location.

## Environmental Exposure to Non-Persistent Endocrine Disrupting Chemicals and Endometriosis: A Systematic Review

2022-05-05

Endometriosis is a disease characterized by the presence of the uterine endometrium outside of its normal location. As the etiology of endometriosis is not well known and hormonal imbalance is central to disease pathogenesis, the potential contribution of exposure to endocrine-disrupting chemicals (EDCs) has been hypothesized in endometriosis. A systematic search of the literature was carried out to identify relevant studies using: PubMed, Scopus, Elsevier, Springer;

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EBSCO, and Web of Science. A total of 22 studies were considered. Most of the studies reviewed in this paper showed an association between exposure to BPA and phthalates and endometriosis. In the case of phthalate exposure, the reviewed studies found an association between the concentration of at least one phthalate metabolite and endometriosis. Only one study was performed to assess the exposure to parabens and a significant relationship with endometriosis was found. Additionally, only one study assessed the relationship of non-persistent pesticide exposure with endometriosis, observing a significant association between endometriosis and the urinary concentration of diazinon, chlorpyrifos, and chlorpyrifos-methyl. Studies struggled to provide a conclusion on the effect of exposure to benzophenones on endometriosis. Despite the numerous limitations of the results, the reviewed studies suggest that exposure to non-persistent endocrine disruptors, especially bisphenol A and phthalates may affect endometriosis. The results of the studies on exposure to parabens, benzophenones, and non-persistent insecticides are inconclusive.

Authors: Katarzyna Wieczorek, Dorota Szczęśna, Joanna Jurewicz

Full Source: International journal of environmental research and public health 2022 May 5;19(9):5608. doi: 10.3390/ijerph19095608.

## ENVIRONMENTAL RESEARCH

### Modeling and Predicting Pulmonary Tuberculosis Incidence and Its Association with Air Pollution and Meteorological Factors Using an ARIMAX Model: An Ecological Study in Ningbo of China

2022-04-28

The autoregressive integrated moving average with exogenous regressors (ARIMAX) modeling studies of pulmonary tuberculosis (PTB) are still rare. This study aims to explore whether incorporating air pollution and meteorological factors can improve the performance of a time series model in predicting PTB. We collected the monthly incidence of PTB, records of six air pollutants and six meteorological factors in Ningbo of China from January 2015 to December 2019. Then, we constructed the ARIMA, univariate ARIMAX, and multivariate ARIMAX models. The ARIMAX model incorporated ambient factors, while the ARIMA model did not. After prewhitening, the cross-correlation analysis showed that PTB incidence was related to air pollution and meteorological factors with a lag effect. Air pollution and meteorological factors also had a correlation. We found

The autoregressive integrated moving average with exogenous regressors (ARIMAX) modeling studies of pulmonary tuberculosis (PTB) are still rare.

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that the multivariate ARIMAX model incorporating both the ozone with 0-month lag and the atmospheric pressure with 11-month lag had the best performance for predicting the incidence of PTB in 2019, with the lowest fitted mean absolute percentage error (MAPE) of 2.9097% and test MAPE of 9.2643%. However, ARIMAX has limited improvement in prediction accuracy compared with the ARIMA model. Our study also suggests the role of protecting the environment and reducing pollutants in controlling PTB and other infectious diseases.

Authors: Yun-Peng Chen, Le-Fan Liu, Yang Che, Jing Huang, Guo-Xing Li, Guo-Xin Sang, Zhi-Qiang Xuan, Tian-Feng He

Full Source: International journal of environmental research and public health 2022 Apr 28;19(9):5385. doi: 10.3390/ijerph19095385.

## PHARMACEUTICAL/TOXICOLOGY

### Metabolic linkages between zinc exposure and lung cancer risk: A nested case-control study

2022-05-10

Epidemiologic studies have suggested that elevated concentrations of zinc are associated with a decreased risk of lung cancer, but the underlying mechanisms remain to be investigated. The metabolites are highly sensitive to environmental stress, which will help to reveal the linkages between zinc exposure and lung cancer risk. We designed a nested case-control study including 101 incident lung cancer cases and 1:2 age- and sex-frequency-matched 202 healthy controls from the Dongfeng-Tongji cohort. Their plasma level of zinc was determined by using inductively coupled plasma-mass spectrometry (ICP-MS) and plasma profiles of metabolites were detected by using an untargeted metabolomics approach. The generalized linear models (GLM) were applied to assess the associations of plasma zinc with metabolites, and the mediation effects of zinc-related metabolites on zinc-lung cancer association were further testified. The concentrations of 55 metabolites had linear dose-response relationships with plasma zinc at a false discovery rate (FDR) < 0.05, among which L-proline, phosphatidylcholine (PC, 34:2), phosphatidylethanolamine (PE, O-36:5), L-altrose, and sphingomyelin (SM, 40:3) showed different levels between lung cancer cases and healthy controls (fold change = 0.92, 0.95, 1.07, 0.90, and 1.08, respectively, and all  $P < 0.05$ ). The plasma concentration of SM(40:3) was negatively associated with incident risk of lung cancer [OR(95%CI) = 0.71(0.55, 0.91),  $P = 0.007$ ] and could mediate 41.7% of the association between zinc and lung cancer risk ( $P = 0.004$ ). Moreover, compared to the traditional factors, addition

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of SM(40:3) exerted improved prediction performance for incident risk of lung cancer [AUC(95%CI) = 0.714(0.654, 0.775) vs. 0.663(0.600, 0.727),  $P = 0.030$ ]. Our findings revealed metabolic profiles with zinc exposure and provide new insight into the alternations of metabolites underpinning the links between zinc exposure and lung cancer development.

Authors: Yansen Bai, Qiang Cao, Xin Guan, Hua Meng, Yue Feng, Chenming Wang, Ming Fu, Shiru Hong, Yuhan Zhou, Fangfang Yuan, Xiaomin Zhang, Meian He, Huan Guo

Full Source: The Science of the total environment 2022 May 10;155796. doi: 10.1016/j.scitotenv.2022.155796.

### Epigenetic Inheritance: Intergenerational Effects of Pesticides and Other Endocrine Disruptors on Cancer Development

2022-04-23

Parental environmental experiences affect disease susceptibility in the progeny through epigenetic inheritance. Pesticides are substances or mixtures of chemicals-some of which are persistent environmental pollutants-that are used to control pests. This review explores the evidence linking parental exposure to pesticides and endocrine disruptors to intergenerational and transgenerational susceptibility of cancer in population studies and animal models. We also discuss the impact of pesticides and other endocrine disruptors on the germline epigenome as well as the emerging evidence for how epigenetic information is transmitted between generations. Finally, we discuss the importance of this mode of inheritance in the context of cancer prevention and the challenges ahead.

Authors: Heloiza Diniz Nicolella, Sonia de Assis

Full Source: International journal of molecular sciences 2022 Apr 23;23(9):4671. doi: 10.3390/ijms23094671.

## OCCUPATIONAL

### The relationship between toluene diisocyanate exposure and respiratory health problems: A meta-analysis of epidemiological studies

2022-05-11

Human epidemiological studies have shown inconclusive results over the effects of diisocyanates on respiratory health problems. A meta-analysis combined evidence on the association between occupational asthma

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(OA), respiratory function, and toluene diisocyanate (TDI) inhalation exposure. Sixty-one articles on occupational toluene diisocyanate exposure were identified via two databases. Fourteen studies were included in the meta-analysis. The Newcastle-Ottawa Scale (NOS) was used to assess the quality of the studies. Odds ratios (OR<sub>asthma</sub>) for the association between TDI exposure compared to non-exposure and OA were calculated. The difference in mean differences (MD) of forced expiratory volume in 1 s (FEV1) and forced vital capacity (FVC), and the annual mean change differences-in milliliters per year (mL/yr)-in FEV1 and FVC pulmonary function between TDI exposed and non-exposed, were calculated. When applicable, a random effects meta-analysis was performed. The overall summary OR<sub>asthma</sub> for TDI exposed versus non-exposed was 1.18 (95% CI = 0.78-1.79). The summary of the predicted mean percentage difference (MD%<sub>predicted</sub>) between exposed versus non-exposed was 2.96% for FEV1 and 3.75% for FVC. A very small decrease of 5 mL/yr for FEV1 and 10 mL/yr for FVC, respectively, was observed between the exposed and the non-exposed groups. There was moderate to low heterogeneity between study results, and most studies were evaluated as high-quality. This meta-analysis found no statistically significant adverse association between TDI occupational exposure and OA. No meaningful differences in lung function were detected between exposed and unexposed groups.

Authors: Evangelia E Antoniou, Maurice P Zeegers

Full Source: Toxicology and industrial health 2022 May 11;7482337221095386. doi: 10.1177/07482337221095386.

### Secondhand Smoke in the Workplace Is Associated With Depression in Korean Workers

2022-04-26

Background: Smoking negatively affects health, and previous studies argue that secondhand smoke (SHS) has a significantly negative health effect. We investigated whether SHS in the workplace influences workers' depression. Methods: Three years of data (2014, 2016, and 2018) from the Korean National Health and Nutrition Examination Survey were analyzed. Participants who were not current smokers were classified into the occupational SHS exposed and non-exposed groups. Multivariate logistic regression was performed to estimate odds ratios (ORs) and 95% confidence intervals (CIs) by adjusting various covariates. Stratified analysis with variables, such as year, sex, occupational classification, average working hours, was additionally performed. Results: The crude ORs of depression was

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1.51 (95% CI: 1.27-1.80), and the fully adjusted OR with all the covariates was 1.57 (95% CI: 1.30-1.88). This indicated a significant relationship between occupational SHS and depression. The ORs increased every 2 years: 1.07 (95% CI: 0.79-1.44) in 2014, 1.88 (95% CI: 1.34-2.64) in 2016, and 2.07 (95% CI: 1.43-2.99) in year 2018. Stratification analysis also showed a significant association between SHS and depression among those in the prolonged work hours group and male employees, as well as blue- and white-collar workers. Conclusion: SHS in the workplace was significantly associated with workers' depression. Our study provides insights into the impact of exposure to SHS for workers and provides a basis for further research and policy-making in this field.

Authors: Seunghan Kim, Juyeon Oh, Byungyoon Yun, Ara Cho, Juho Sim, Jin-Ha Yoon

Full Source: *Frontiers in public health* 2022 Apr 26;10:802083. doi: 10.3389/fpubh.2022.802083.

### Assessment of occupational and dietary exposures of feed handling workers to mycotoxins in rural areas from São Paulo, Brazil

2022-05-10

In the current study, the occupational and dietary exposures of feed handling workers (N = 28) to aflatoxins (AFs), fumonisins (FBs), ochratoxin A (OTA), deoxynivalenol (DON), zearalenone (ZEN), toxins T-2 and HT-2 were assessed for the first time in animal-producing farms and feed factories from São Paulo, Brazil. Mycotoxins in food (n = 244) and airborne dust (n = 27), as well as biomarkers in urine (n = 97) samples were determined by liquid chromatography coupled with tandem mass spectrometry. FBs were detected in all airborne dust samples, with concentrations ranging from 7.85 to 16,839 ng/m<sup>3</sup>. The mean probable daily intake (PDI) based on food data were 0.005, 0.769, 0.673 and 0.012 µg/kg of body weight (bw)/day for AFs, FBs, DON and ZEN, respectively. Mean PDI values obtained through urinary biomarkers were 0.29, 0.10, 0.50, 9.72 and 0.10 µg/kg body weight/day for AFB<sub>1</sub>, DON, OTA, FB<sub>1</sub> and ZEN, respectively. The analyses based on urinary biomarkers revealed a potential health concern for OTA and FBs, although no potential health concern was observed with PDI calculated through food data. Results of this trial stress the need for preventive measures to avoid health risks of workers in Brazilian animal-producing farms and feed industries.

Authors: Larissa T Franco, Carlos A F Oliveira

Full Source: *The Science of the total environment* 2022 May 10;155763. doi: 10.1016/j.scitotenv.2022.155763.

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### Whole Body Vibration Exposure Transmitted to Drivers of Heavy Equipment Vehicles: A Comparative Case According to the Short- and Long-Term Exposure Assessment Methodologies Defined in ISO 2631-1 and ISO 2631-5

2022-04-25

The construction and transport sectors are the industries with the highest proportions of workers exposed to vibrations in the European Union. Heavy equipment vehicle (HEV) drivers often perform operations on different uneven surfaces and are exposed to whole body vibration (WBV) on a daily basis. Recently, a new version of ISO 2631-5 was published. However, since this new method required as input the individual exposure profile and the acceleration signals recorded on more surfaces, limited studies have been carried out to evaluate HEV operations according to this standard. The objectives of this study were to assess the WBV exposure using the methods defined in ISO 2631-1:1997 and ISO 2631-5:2018 and to compare the obtained health risk assessments between drivers with different anthropometric characteristics. For this purpose, two drivers were selected and a field measurement campaign was conducted. Regarding short-term assessment, results showed that VDV was the most restrictive method with exposure levels above the exposure action limit value, while SdA indicated that the same exposures were safe for the worker. With respect to long-term assessment, Risk Factor RA showed that the driver with the highest body mass index was the only one who exceeded the low probability limit of adverse health effects.

Authors: María L de la Hoz-Torres, Antonio J Aguilar, Diego P Ruiz, M<sup>a</sup> Dolores Martínez-Aires

Full Source: *International journal of environmental research and public health* 2022 Apr 25;19(9):5206. doi: 10.3390/ijerph19095206.

The construction and transport sectors are the industries with the highest proportions of workers exposed to vibrations in the European Union.