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# Preface

This issue is devoted to the abstracts of the presentations for the Continuing Education courses and Scientific Sessions of the 62nd Annual Meeting of the Society of Toxicology, at the Music City Center, Nashville, Tennessee, March 19–23, 2023.

An alphabetical Author Index, cross-referencing the corresponding abstract number(s), begins on page 511.

The issue also contains a Keyword Index (by subject or chemical) of all the presentations, beginning on page 547.

The abstracts are reproduced as accepted by the Scientific Program Committee of the Society of Toxicology and appear in numerical sequence. If a number is missing in the numerical sequence, the abstract assigned to the missing number was withdrawn by the author(s). Author names that are underlined in the author block indicate that the author is a member of the Society of Toxicology. For example, J. Smith. SOT members may sponsor abstracts that do not include an author with SOT membership. Authors who are members of designated organizations could serve as the sponsor of the abstract if an SOT member was not a co-author; these types of sponsorships are displayed with an organization name after the sponsor name (e.g., Sponsor: A. Smith, EUROTOX).

*Scientific Session Types:*

- CE Continuing Education Courses
- EC Education-Career Development Sessions
- IS Informational Sessions
- PL Platform Sessions
- PS Poster Sessions
- R Roundtable Sessions
- S Symposium Sessions
- W Workshop Sessions

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show that the oxygenated terpenes behave similarly to biosurfactants and other detergent like products resulting in decreased membrane permeability. The results of this study show the changes that terpenes undergo during vaping and how they induce the formation of more degradation products of the e-liquid solvents, which leads to increased membrane permeability. Terpene additives increase membrane permeability through oxidation of terpenes and increased degradation products of MCT oil. These findings are a steppingstone to better understanding the cytotoxic effects of terpenes in vaping products.

### 3469 Toward Developing Novel Prostate Cancer Recurrence Suppressors: Acute and Subchronic Toxicity of Pseurotin A, an Orally Active PCSK9 Axis–Targeting Small Molecule, in Swiss Albino Mice

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Proprotein convertase subtilisin kexin type 9 (PCSK9) emerged as a therapeutic target of great interest in cancer and cardiovascular diseases due to its ability to induce LDL-cholesterol by preventing LDL receptor (LDLR) recycling. Preliminary studies revealed that pseurotin A (PSA), a spiro-heterocyclic γ-lactam alkaloid from several *Aspergillus* and *Penicillium* species, can modulate the oncogenic role of PCSK9 in breast and prostate cancers progression and recurrence due to its dual ability to suppress PCSK9 expression and protein-protein interaction (PPI) with LDLR. Thus, a preliminary assessment of PSA acute toxicity represents an important step to developing PSA as a novel orally active PCSK9 axis-modulating cancer recurrence inhibitor. Male and female Swiss albino mice administered by oral gavage PSA single doses of 10, 250, and 500 mg/kg for the acute toxicity study and daily doses at 10, 40, and 80 mg/kg over 3 months for the sub-chronic study versus vehicle controls. Mice continuously observed over the experiments course to monitor any abnormalities in their behavioral, neuromuscular, and autonomic responses. Mice sacrificed at each study end, their body and organ weights recorded and collected. Mice plasma samples subjected to comprehensive hematological and biochemical analyses. Collected mouse organs histopathologically analyzed. No morbidity detected following any PSA oral dosing. The Up-and-Down methodology determined PSA $LD_{50}$ value of >550 mg/kg. No observed histopathological abnormalities in liver, kidney, brain, and heart, suggesting a high safety profile as a prospective valid lead for future use as a first-in-class small molecule prostate cancer recurrence suppressor via PCSK9 axis modulation.

### 3470 Evaluation of the Effect of Orally Administered Histacel Extract on Respiratory Functions on Anaphylactic Shock in Male Wistar Rats

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Anaphylaxis is a life-threatening form of hypersensitivity characteterised by the activation of mast cells and basophils, resulting in release of biochemical mediators that influence vascular permeability. The present study was undertaken to explore the antiasthmatic activity of histacel extract (poly herbal extract). This study was conducted to evaluate the effect of histacel extract on the respiratory function in conscious male rats following repeated gavage administration for 14 days using whole body plethysmography. The test item and Montelukast were administered once daily through gavage for 14 days to rats belonging to three treatment groups (G3 - G5) and a positive control (G6) group, respectively. Rats (G2 to G6) were immunised by 0.5 mL SC injection of dTpa vaccine and horse serum. Rats belonging to the vehicle and the sensitised control groups received RO water. Rats were observed daily for mortality and clinical signs. Respiratory parameters like respiratory rate, tidal volume, minute volume, etc., were recorded after the treatment on days 0, 7, and 14 for 3 hours, 1 hour, and 30 minutes respectively. Rats were challenged on treatment day 14 by a 1 mL IV injection of horse serum. Rats were observed for respiratory functions immediately after the challenge injection for 20 minutes. The test item at mid (250 mg/kg b. wt./day) and high (500 mg/kg b. wt./day) doses caused an increase in the tidal volume, minute ventilation, and a decrease in the frequency of respiration, post-challenge with horse serum. Thus improving the respiratory function in the anaphylactic shock-induced male Wistar rats. Similar effects were observed in the respiratory function for the Montelukast (positive control) administered group, post-challenge with horse serum. The findings of the study suggest that histacel extract has an anti-anaphylactic activity as it improves the respiratory functions in the experimental models, similar to Montelukast, a known anti-allergic compound.

### 3471 Toxicity of the Insensitive Explosive FOX-7 in Sprague Dawley Rats via Oral Gavage

M. Bohannon, L. Crouse, and B. Guigni. *Army Public Health Center, Gunpowder, MD.*

The insensitive explosive 1,1-diamino-2,2-dinitroethene (DADNE, referred to as FOX-7) is a bright yellow, crystalline powder developed by the Swedish military in the late 1990s. Compared to the legacy explosive RDX, FOX-7 shows significant improvements in response to impact and friction stimuli while maintaining nearly equal performance. A complete oral toxicological test series in rats is currently being performed to assess the toxicity of FOX-7 prior to its use by the U.S. Army. Acute oral studies yielded estimated median lethal doses of 875 (708-1082) mg/kg in male rats and 805 (668-971) mg/kg in female rats. Gross pathological evaluation indicated delayed clearance and moderate irritation throughout the gastrointestinal tract at higher doses. To determine subacute oral toxicity, rats were repeatedly exposed to FOX-7 at 0, 6.25, 12.5, 25, 50, 100, 200, and 400 mg/kg-d for 14 days via oral gavage. No rats in the 200- and 400-mg/kg-d groups survived. Weight loss, irritability, lethargy, and porphyrin staining were frequently observed prior to death or moribund euthanasia. Distended stomachs and evidence of moderate to severe irritation throughout the gastrointestinal tract were found in the majority of the pre-term deaths. Body weight gain in the male 100 mg/kg-d group was lower than controls throughout the treatment period although food consumption was only decreased from days 0 through 7. Kidney and spleen weights were elevated in 100 mg/kg-d males and females. Differences in clinical pathology parameters were mainly confined to the 100 mg/kg-d group. Blood urea nitrogen/creatinine ratios in male rats and alkaline phosphatase concentrations in female rats both exhibited dose-dependent increases. The micronucleus assay was performed on 25, 50, and 100 mg/kg-d male rats, and the results indicated that FOX-7 is not genotoxic in rat peripheral blood at the doses tested. The FOX-7 subchronic oral study has not been initiated to date, but limited results should be available for the conference. These studies are critical to determining safety thresholds for use of FOX-7 by US Army soldiers.

### 3472 Evaluation of Antioxidant Activities of Brown Macroalga *Bifurcaria bifurcata* Extract

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Research in natural products of marine algae has made significant advances in recent years and marine algae have been proven to produce a variety of compounds and some of them have been shown to possess biological activity of potential nutritional and medicinal value. Epidemiological evidence demonstrated that the consumption of marine algae has lowered the occurrence of chronic diseases, such as hypertension, type 2 diabetes, hyperlipidemia, and coronary heart disease which are in part caused by oxidative stress. The aim of this research was to evaluate the response of brown seaweed *Bifurcaria bifurcata* extract to an oxidative stressor, *tert*-butyl hydroperoxide (*tert*-BOOH), in Caco-2 cells. Selected seaweed represents common specie in northern Atlantic coasts of Spain. This study demonstrates that seaweed *B. bifurcata* extract has the ability to protect human colon carcinoma Caco-2 cells against oxidative insult by modulating reactive oxygen species (ROS) generation, malondialdehyde (MDA) production, antioxidant enzymes [NADPH quinone dehydrogenase 1 (NQO1), glutathione S-transferase (GST)] activities, and caspase 3/7 essential enzyme during apoptosis. These results show that treatment of Caco-2 cells in culture with *B. bifurcata* extract confers a significant protection against an oxidative insult and suggest that the seaweed *B. bifurcata* extract can be used as a natural antioxidant in the food industry as well as dietary supplement against oxidative damage. *This work was supported by the Project Ref. PID 2020-15979RR-C33 from the Ministerio de Ciencia e Innovación, Spain.*

### 3473 *In Silico* Occupational Exposure Banding Framework for Data-Poor Compounds in Biotechnology

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Occupational exposure limits (OELs) and occupational exposure bands (OEBs) are exposure benchmarks intended for the protection of worker health. OEBs are typically assigned when there is not sufficient data to derive a quantitative OEL. OEB assignments are typically based on defined methodology and industry best practices often relying on empirical data. However, there is no harmonized methodology available to assign OEBs for compounds with little to no data. Thus, an *in silico* framework approach for OEB assignment was developed for compounds lacking *in vivo* toxicology data. Existing tools, including quantitative structure-activity relationship (QSAR) tools and the NIOSH occupational exposure banding tool, were adapted and used in sequence to assign OEBs to data poor compounds. Briefly, two QSAR tools were used to evaluate standard toxicological endpoints and the results were assigned a reliability rating based on agreement between the QSAR tools. Subsequently, a hazard category per Global Harmonization System (GHS)