

# Bulletin Board

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## CHEMICAL EFFECTS

**Four-week inhalation toxicity study of 1-propanol in F344 rats**

2020-01-20

1-Propanol is used as a solvent for waxes, vegetable oils, resins, cellulose esters, and ethers, and is not considered harmful to humans by food and non-occupational exposures. However, workers are potentially exposed to 1-propanol by inhalation when it is used in the workplace. Thus, inhalation toxicity data are needed to assess the hazard of 1-propanol for workers safety. Five male and five female F344 rats were exposed to 1-propanol vapor for 4-weeks (6 h/day, 5 days/week) at concentrations of 0, 100, 400, and 1600 ppm in a whole-body inhalation chamber system. The actual exposure concentrations were  $100.11 \pm 5.10$ ,  $403.19 \pm 12.31$ , and  $1598.08 \pm 139.58$  ppm for the low, middle, and high dose groups, respectively. No clinical signs, significant mean body weight changes, significant changes of hematology or blood biochemistry results, or histopathological abnormalities were seen related to exposure to the test substance. Under the conditions of this study, the no-observed-adverse-effect level of 1-propanol was over 1600 ppm.

Authors: Yong-Soon Kim, Eun-Sang Cho, Ka-Young Park, Cheol-Hong Lim  
Full Source: Toxicological research 2020 Jan 20;36(4):285-292. doi: 10.1007/s43188-019-00033-1.

**Toxicity and deleterious effects of Artemisia annua essential oil extracts on mulberry pyralid (Glyphodes pyloalis)**

2020-11

Botanical extracts are an important source of bio-pesticides and are generally considered safe to the environment. Artemisia annua L, a medicinal plant, well known for its antimalarial potential, was evaluated as a source of a type of essential oil collected during vegetative growth stage against Glyphodes pyloalis Walker. The main chemical components of the essential oil at vegetative stage of Artemisia annua was analyzed by GC-MS and contained 1,8-cineole (18.68%), Camphor (11.4%),  $\alpha$ -Pinene (9.3%) and 3-Carene (6.3%). The LC50 of this plant oil was estimated to be 0.652% W/V and 2.585  $\mu$ L/L air incorporated orally and fumigation, respectively. The digestive enzymes such as  $\alpha$ -amylases, Proteases, Lipases and  $\beta$ - and  $\gamma$ -glucosidases were considerably inhibited in treated larvae compared with controls. Similarly, the amount of protein, glucose, and

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triglyceride were decreased in the treated larvae by methods used. The lower hemocyte numbers, nodule formation and activity of phenoloxidases after injection of Beauveria bassiana and latex beads showed its EO effect on immunity. The anatomy of the larval midgut after treatment showed degeneration in digestive cells. Emerging adult's ovaries showed significant changes in the ovarian sheath and lack of yolk spheres. The present investigation in accordance with our previous studies may ultimately lead to a formulation in controlling this notorious pest especially in mulberry orchards where the use of conventional chemicals is restricted.

Authors: Marziyeh Oftadeh, Jalal Jalali Sendi, Asgar Ebadollahi  
Full Source: Pesticide biochemistry and physiology 2020 Nov;170:104702. doi: 10.1016/j.pestbp.2020.104702.

## ENVIRONMENTAL RESEARCH

**Valorisation of Fruits, their Juices and Residues into Valuable (Nano)materials for Applications in Chemical Catalysis and Environment**

2020-09-29

One of the most abundant wastes from all around the world is nutrient resources. Among them, fruits, their extracts, and residues comprise a major portion, which contain many valuable components that get lost during disposal or become burden on the shrinking landfills. These concerns are addressed by seeking sustainable processing methods that would have a minimal environmental impact. The crops contain renewable chemicals which are useful for catalysis, wastewater treatment, or preparation of nanomaterials; there has been an upsurge for the industrial applications of (nano)materials as their environmental and catalytic appliances is a fascinating subject to design cheaper and safer catalytic systems. Due to the excellent chemical properties of the fruit extracts, they have garnered attention as cost-effective catalysts and support materials. This review focuses on the preparation of (nano)materials and their catalytic and environmental applications and highlights the potential appliances and industrial benefits derived from these low-cost renewable and sustainable greener sources thus essentially converting waste into wealth.

Authors: Mahmoud Nasrollahzadeh, Nasrin Shafiei, Zahra Nezafat, Nayyereh Sadat Soheili Bidgoli, Fahimeh Soleimani, Rajender S Varma  
Full Source: Chemical record (New York, N.Y.) 2020 Sep 29. doi: 10.1002/tcr.202000078.

**One of the most abundant wastes from all around the world is nutrient resources.**

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**Rethinking Environmental Carcinogenesis**

2020-10

The 2010 report of the President's Cancer Panel concluded that the burden of cancer from chemical exposures is substantial, while the programs for testing and regulation of carcinogens remain inadequate. New research on the role of early life exposures and the ability of chemicals to act via multiple biological pathways, including immunosuppression, inflammation, and endocrine disruption as well as mutagenesis, further supports the potential for chemicals and chemical mixtures to influence disease. Epidemiologic observations, such as higher leukemia incidence in children living near roadways and industrial sources of air pollution, and new in vitro technologies that decode carcinogenesis at the molecular level, illustrate the diverse evidence that primary prevention of some cancers may be achieved by reducing harmful chemical exposures. The path forward requires cross-disciplinary approaches, increased environmental research investment, system-wide collaboration to develop safer economic alternatives, and community engagement to support evidence-informed action. Engagement by cancer researchers to integrate environmental risk factors into prevention initiatives holds tremendous promise for reducing the rates of disease. See all articles in this CEBP Focus section, "Environmental Carcinogenesis: Pathways to Prevention."

Authors: Margaret Kripke, Julia Green Brody, Ernest Hawk, Amanda B Hernandez, Polly J Hoppin, Molly M Jacobs, Ruthann A Rudel, Timothy R Rebbeck

Full Source: Cancer epidemiology, biomarkers & prevention : a publication of the American Association for Cancer Research, cosponsored by the American Society of Preventive Oncology 2020 Oct;29(10):1870-1875. doi: 10.1158/1055-9965.EPI-20-0541.

**Hazardous air pollutants and telomere length in the Sister Study**

2019-08

Background: Telomeres are vital for genomic integrity and telomere length has been linked to many adverse health outcomes. Some hazardous air pollutants, or air toxics, increase oxidative stress and inflammation, two possible determinants of shortened telomere length. No studies have examined air toxic-telomere length associations in a non-occupational setting.

Methods: This study included 731 Sister Study participants (enrolled 2003-2007) who were randomly selected to assess telomere length in

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baseline blood samples. Multiplex qPCR was used to determine telomere to single copy gene (T/S) ratios. Census tract concentration estimates of 29 air toxics from the 2005 National Air Toxics Assessment were linked to baseline residential addresses. Air toxics were classified into tertile-based categories of the exposure. Multivariable linear regression was used to estimate  $\beta$  coefficients and 95% confidence intervals (CI) in single pollutant models. Multipollutant groups were identified with regression trees.

Results: The average T/S ratio was 1.24. Benzidine (T3vsT1  $\beta$ = -0.08; 95% CI: -0.14, -0.01) and 1,4-dioxane (T3vsT1  $\beta$ = -0.06; 95% CI: -0.13, 0.00) in particular, as well as carbon tetrachloride, chloroprene, ethylene dibromide, and propylene dichloride, were associated with shorter relative telomere length. Benzidine (p=0.02) and 1,4-dioxane (p=0.06) demonstrated some evidence of a monotonic trend. The regression tree identified age, BMI, physical activity, ethylene oxide, acrylonitrile, ethylidene dichloride, propylene dichloride, and styrene in multipollutant groups related to telomere length.

Conclusions: In this first study of air toxics and telomere length in a non-occupational setting, several air toxics, particularly 1,4-dioxane and benzidine, were associated with shorter relative telomere length.

Authors: Nicole M Niehoff, Marilie D Gammon, Alexander P Keil, Hazel B Nichols, Lawrence S Engel, Jack A Taylor, Alexandra J White, Dale P Sandler

Full Source: Environmental epidemiology (Philadelphia, Pa.) 2019 Aug;3(4):e053. doi: 10.1097/ee9.000000000000053.

**OCCUPATIONAL****Estimates of Occupational Inhalation Exposures to Six Oil-Related Compounds on the Four Rig Vessels Responding to the Deepwater Horizon Oil Spill**

2020-10-03

Background: The 2010 Deepwater Horizon (DWH) oil spill involved thousands of workers and volunteers to mitigate the oil release and clean-up after the spill. Health concerns for these participants led to the initiation of a prospective epidemiological study (GuLF STUDY) to investigate potential adverse health outcomes associated with the oil spill response and clean-up (OSRC). Characterizing the chemical exposures of the OSRC workers was an essential component of the study. Workers on the four oil rig vessels mitigating the spill and located within a 1852

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m [1 nautical mile] radius of the damaged wellhead [the Discoverer Enterprise (Enterprise), the Development Driller II (DDII), the Development Driller III (DDIII), and the Helix Q4000] had some of the greatest potential for chemical exposures.

**Objectives:** The aim of this paper is to characterize potential personal chemical exposures via the inhalation route for workers on those four rig vessels. Specifically, we presented our methodology and descriptive statistics of exposure estimates for total hydrocarbons (THCs), benzene, toluene, ethylbenzene, xylene, and n-hexane (BTEX-H) for various job groups to develop exposure groups for the GuLF STUDY cohort.

**Methods:** Using descriptive information associated with the measurements taken on various jobs on these rig vessels and with job titles from study participant responses to the study questionnaire, job groups [unique job/rig/time period (TP) combinations] were developed to describe groups of workers with the same or closely related job titles. A total of 500 job groups were considered for estimation using the available 8139 personal measurements. We used a univariate Bayesian model to analyze the THC measurements and a bivariate Bayesian regression framework to jointly model the measurements of THC and each of the BTEX-H chemicals separately, both models taking into account the many measurements that were below the analytic limit of detection.

**Results:** Highest THC exposures occurred in TP1a and TP1b, which was before the well was mechanically capped. The posterior medians of the arithmetic mean (AM) ranged from 0.11 ppm ('Inside/Other', TP1b, DDII; and 'Driller', TP3, DDII) to 14.67 ppm ('Methanol Operations', TP1b, Enterprise). There were statistical differences between the THC AMs by broad job groups, rigs, and time periods. The AMs for BTEX-H were generally about two to three orders of magnitude lower than the THC AMs, with benzene and ethylbenzene measurements being highly censored.

**Conclusions:** Our results add new insights to the limited literature on exposures associated with oil spill responses and support the current epidemiologic investigation of potential adverse health effects of the oil spill.

**Authors:** Tran B Huynh, Caroline P Groth, Gurumurthy Ramachandran, Sudipto Banerjee, Mark Stenzel, Harrison Quick, Aaron Blair, Lawrence S Engel, Richard K Kwok, Dale P Sandler, Patricia A Stewart

**Full Source:** Annals of work exposures and health 2020 Oct 3;wxaa072. doi: 10.1093/annweh/wxaa072.

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### Assessment of occupational exposure to fine particulate matter in dental prosthesis laboratories in Kocaeli, Turkey

2020-10-01

Dental prosthesis laboratories (DPLs) are among the workplaces where predominantly manual production takes place. In such working environments, during the manual manufacturing process, which involves fine smoothing and polishing of dental prostheses, fine particulate matter is released into the ambient air. In this study, the particulate matter (PM) concentrations and elemental content of the fine particles in the working ambient air were identified in six DPLs in Kocaeli, Turkey. PM<sub>2.5</sub> mass concentrations, measured in all the DPLs, ranged between 80.8 and 1645 µg/m<sup>3</sup> (mean 414 ± 406). As a result of the analyses performed with an ICP-MS device (Perkin Elmer Elan@DRC-e), trace elements of Be, Cd, Hg, and, notably, Co, Cr, Mo, and Ni were found. The researchers calculated the excess lifetime cancer risks and total hazard indexes. The average total cancer risk for all the DPLs was 8 × 10<sup>-3</sup>, which is higher than the acceptable limit of 1.0 × 10<sup>-6</sup>, and the total hazard index was 187, which is greater than the acceptable limit of 1.0. Considering these high-level risks, the study concluded that there is a need for new production methods, and strict application of occupational health and safety measures, to reduce the fine particle exposure of the workers in the laboratories. In addition, there are prescribed limit values for particulate matter only for respirable particles in working environments. The establishment of limit values, especially for PM<sub>2.5</sub> concentrations, is important for the protection of the health of the employees.

**Authors:** Serap Aarsal Yildirim, Beyhan Pekey, Hakan Pekey

**Full Source:** Environmental monitoring and assessment 2020 Oct 1;192(10):667. doi: 10.1007/s10661-020-08620-8.

### Respiratory Health and Inflammatory Markers-Exposure to Cobalt in the Swedish Hard Metal Industry

2020-10

**Objective:** To study the relationship between inhalable dust and cobalt, and respiratory symptoms, lung function, exhaled nitric oxide in expired air, and CC16 in the Swedish hard metal industry.

**Methods:** Personal sampling of inhalable dust and cobalt, and medical examination including blood sampling was performed for 72 workers. Exposure-response relationships were determined using logistic, linear, and mixed-model analysis.

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**Results:** The average inhalable dust and cobalt concentrations were 0.079 and 0.0017 mg/m, respectively. Statistically significant increased serum levels of CC16 were determined when the high and low cumulative exposures for cobalt were compared. Nonsignificant exposure-response relationships were observed between cross-shift inhalable dust or cobalt exposures and asthma, nose dripping, and bronchitis.

**Conclusions:** Our findings suggest an exposure-response relationship between inhalable cumulative cobalt exposure and CC16 levels in blood, which may reflect an injury or a reparation process in the lungs.

**Authors:** Lena Andersson, Alexander Hedbrant, Ing-Liss Bryngelsson, Alexander Persson, Anders Johansson, Annette Ericsson, Per Vihlborg, Bengt Sjögren, Eva Särndahl, Leo Stockfelt, Håkan Westberg

**Full Source:** Journal of occupational and environmental medicine 2020 Oct;62(10):820-829. doi: 10.1097/JOM.0000000000001952.

## PHARMACEUTICAL/TOXICOLOGY

### Contamination, suffering and womanhood: Lay explanations of breast cancer in Central Vietnam

2020-09-12

Breast cancer has become the most frequent cancer among women in Vietnam, claiming over 6000 lives a year. In this article we investigate how laypeople explain the causes of this pressing health issue based on an ethnographic study conducted in the Central region of Vietnam in 2019, including hospital observation, interviews with 33 breast cancer patients and focus groups with 21 laypeople. Our findings show that their knowledge of causation is mediated through historical social contexts of warfare, a rapacious market economy, poverty, and cultural configurations of gender roles. Contamination of the environment and food, use of chemicals, failure to follow postpartum practices, breast ailments, and worry are understood to be immediate determinants of breast cancer. These popular accounts are unlikely to recognize biomedical narratives of breast cancer risk that focus upon individual responsibility and lifestyle factors because they may not reflect the lived realities of women. We emphasise the implications for public awareness campaigns to meaningfully engage with the situated social and cultural specificities of breast cancer.

**Authors:** Trang Thu Do, Andrea Whittaker

**Full Source:** Social science & medicine (1982) 2020 Sep 12;266:113360. doi: 10.1016/j.socscimed.2020.113360.

**Breast cancer has become the most frequent cancer among women in Vietnam, claiming over 6000 lives a year.**

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### Phase II study of atezolizumab in combination with bevacizumab in patients with advanced cervical cancer 2020-10

**Background:** There are limited treatment options for patients with metastatic or recurrent cervical cancer. Platinum-based chemotherapy plus the anti-vascular endothelial growth factor antibody bevacizumab remains the mainstay of advanced treatment. Pembrolizumab is Food and Drug Agency approved for programmed death ligand 1 (PD-L1) positive cervical cancer with a modest response rate. This is the first study to report the efficacy and safety of the PD-L1 antibody atezolizumab in combination with bevacizumab in advanced cervical cancer.

**Methods:** We report the results from a phase II, open-label, multicenter study (NCT02921269). Patients with advanced cervical cancer were treated with bevacizumab 15 mg/kg intravenous every 3 weeks and atezolizumab 1200 mg intravenous every 3 weeks. The primary objective was to measure the objective response rate (ORR). Secondary endpoints included disease control rate (DCR), progression-free survival (PFS), overall survival (OS), and safety.

**Results:** In the total evaluable population (n=10), zero patients achieved an objective response as assessed by Response Evaluation Criteria In Solid Tumors (RECIST) V.1.1, resulting in a confirmed ORR of 0%. Of note, there were two patients who achieved an unconfirmed PR. The DCR by RECIST V.1.1 was 60% (0% complete response, 0% partial response, 60% stable disease). Median PFS was 2.9 months (95% CI, 1.8 to 6) and median OS was 8.9 months (95% CI, 3.4 to 21.9). Safety results were generally consistent with the known safety profile of both drugs, notably with two high-grade neurologic events.

**Conclusions:** The combination of bevacizumab and atezolizumab did not meet the predefined efficacy endpoint, as addition of bevacizumab to PD-L1 blockade did not appear to enhance the ORR in cervical cancer.

**Authors:** Claire F Friedman, Alexandra Snyder Charen, Qin Zhou, Michael A Carducci, Alexandre Buckley De Meritens, Bradley R Corr, Siqing Fu, Travis J Hollmann, Alexia Iasonos, Jason A Konner, Panagiotis A Konstantinopoulos, Susan C Modesitt, Elad Sharon, Carol Aghajanian, Dmitriy Zamarin

**Full Source:** Journal for immunotherapy of cancer 2020 Oct;8(2):e001126. doi: 10.1136/jitc-2020-001126.

**Background: There are limited treatment options for patients with metastatic or recurrent cervical cancer.**