Response to reviewer comments

Dear Dr. Laura Jurecska

2/6/2025

I would like to express my heartfelt gratitude for the opportunity to receive comments on my dissertation. I sincerely appreciate the time, effort, and expertise that the Dr. Laura Jurecska have dedicated to evaluating my work. Her thoughtful and constructive feedback has been invaluable in strengthening the quality, clarity, and academic rigor of my work.

1- Why did you choose the USEPA's ILCR model to estimate the human cancer risk posed by exposure to environmental PAHs? Are there other available models for the assessment of health effects of these compounds?

Response

Thank you very much for bringing up this important question. According to the literature, the USEPA's Incremental Lifetime Cancer Risk (ILCR) model is widely utilized to assess the potential cancer risk associated with exposure to carcinogenic polycyclic aromatic hydrocarbons (PAHs). This model estimates the probability that an individual will develop cancer over a lifetime as a result of exposure to these hazardous compounds. In addition to the USEPA ILCR model, there are several alternative models used for PAHs health risk assessment. Below is an overview of some of these alternative models, including their descriptions, advantages, and disadvantages:

Alternative Models for PAHs Health Risk Assessment

Model	**Description**	**Advantages**	**Disadvantages**
USEPA ILCR Model	Estimates cancer risk based on lifetime exposure and slope factors.	Widely used, regulatory acceptance, straightforward calculation.	Does not account for variability in metabolism or individual susceptibility.

Monte Carlo Simulation	Uses probability distributions instead of fixed values to model uncertainty.	Provides more realistic risk estimates, accounts for population variability.	Requires computational resources, data-intensive.
Benzo[a]pyrene Equivalency (BaPeq) Model	Converts PAH concentrations to BaP equivalents using Toxic Equivalency Factors (TEFs).	Standardizes PAH toxicity, simplifies risk assessment.	TEFs are based on experimental data, may not reflect real-world metabolism.
Physiologically Based Pharmacokinetic (PBPK) Model	Simulates PAH absorption, distribution, metabolism, and excretion in the human body.	Mechanistic approach, considers biological variability.	Complex, requires extensive physiological and toxicokinetic data.
Margin of Exposure (MOE) Model	Compares PAH exposure levels to benchmark doses from toxicological studies.	Useful for risk prioritization, does not require cancer slope factors.	Does not provide explicit probability of cancer risk.

Comparison Summary

- **USEPA ILCR Model** is simple and widely accepted but lacks individual variability considerations.
- **Monte Carlo Simulation** improves uncertainty analysis but is computationally demanding.
- **BaPeq Model** simplifies PAH toxicity estimation but relies on estimated TEFs.
- **PBPK Models** provide detailed biological insights but require extensive data.
- **MOE Model** helps prioritize risk but does not estimate actual cancer probabilities.

References

Rajasekhar, Bokam, Indumathi M. Nambi, and Suresh Kumar Govindarajan. "Human health risk assessment of ground water contaminated with petroleum PAHs using Monte Carlo simulations: a case study of an Indian metropolitan city." *Journal of environmental management* 205 (2018): 183-191.

Zhao, Ping, et al. "Applications of physiologically based pharmacokinetic (PBPK) modeling and simulation during regulatory review." *Clinical Pharmacology & Therapeutics* 89.2 (2011): 259-267.

Benford, Diane, Michael DiNovi, and R. Woodrow Setzer. "Application of the margin-of-exposure (MoE) approach to substances in food that are genotoxic and carcinogenic eg: benzo [a] pyrene and polycyclic aromatic hydrocarbons." *Food and Chemical Toxicology* 48 (2010): S42-S48.

Famiyeh, Lord, et al. "A review on analysis methods, source identification, and cancer risk evaluation of atmospheric polycyclic aromatic hydrocarbons." *Science of the Total Environment* 789 (2021): 147741.

2- Please, provide a more detailed explanation, why PAH content of Tigris River sediment samples are different from sediment samples of Danube and Euphrate in terms of correlation with TOM (total organic matter) content (Figure 28)?

Response

Thank you very much for this insightful and valuable question. The contrasting correlation patterns between total organic matter (TOM) and PAH concentrations in the sediments of the Tigris River, compared to the Danube and Euphrates Rivers, are attributable to fundamental differences in the sources, distribution mechanisms, and environmental interactions of PAHs across these river systems. In the Danube and Euphrates Rivers, Figure 28 illustrates a strong positive correlation between TOM and PAH concentrations. In such systems, PAHs tend to exhibit a geochemically mediated distribution, with gradual accumulation in sediments proportional to the local organic content. This relationship suggests a dominant influence of diffuse, non-point sources such as atmospheric deposition, urban runoff, and industrial discharges, which contribute to a homogenized contaminant profile that strongly reflects the organic matrix.

In contrast, the Tigris River shows a weak correlation between PAHs and TOM, suggesting that sedimentary PAH distribution is driven not by geochemical affinity to organic matter, but rather by spatially concentrated, point-source discharges. As detailed in the thesis, sediment samples from the Tigris were collected in close proximity to major oil refineries and combustion sources. These facilities discharge untreated effluent directly into the river, introducing PAHs into the sediment regardless of the TOM content.

Moreover, the types of PAHs identified in the Tigris River predominantly high molecular weight (HMW) compounds which are more persistent and less likely to be biodegraded or dispersed. These compounds typically result from high-temperature combustion and exhibit limited mobility. Therefore, they tend to accumulate rapidly and heterogeneously in sediments near their point of release, rather than dispersing and equilibrating with organic matter across a broader area.

Other studies conducted worldwide have also reported no correlation. For example:

1- *"However, no correlation was found between EPAHs and organic carbon content in the harbour sediments (correlation coefficient of 0.327)." (*__Mostafa__ et al., 2003)

*"the distribution and concentrations of PAHs in sediments would be determined more by direct input, rather than by the type of sediment found locally." (*__Mostafa__ et al., 2003)

Mostafa, Alaa R., et al. "Composition, distribution and sources of polycyclic aromatic hydrocarbons in sediments of the western harbour of Alexandria, Egypt." *Journal of Soils and Sediments* 3 (2003): 173-179.

2- *"However, a poor correlation was found between TOC and PAH concentrations in this study (Figure 5a, R = 0.30)." (*__Wang__ et al., 2014).

Wang, Zucheng, et al. "Concentrations and sources of polycyclic aromatic hydrocarbons in surface coastal sediments of the northern Gulf of Mexico." *Geochemical transactions* 15 (2014): 1-12.

3- *"in current research, no correlation was observed between PAHs and TOM (r = 0.09, P > 0.05) (Fig. 3)"* (**Cheraghi** et al., 2025)

Cheraghi, Mitra, et al. "Investigating Oil Entrance from Hendijan Oil Field in the Northwest of the Persian Gulf Using Chemical Fingerprinting." *Archives of Environmental Contamination and Toxicology* 88.1 (2025): 76-96.

Other studies conducted worldwide have reported positive correlations. For example:

*1- "A significant correlation was found in the present study between total organic matter (TOM), grain size and PAHs" (***Younis** et al., 2018)

Younis, Alaa M., et al. "Assessment of polycyclic aromatic hydrocarbons in surface sediments and some fish species from the Gulf of Suez, Egypt." *Egyptian Journal of Aquatic Biology and Fisheries* 22.4 (2018): 49-59.

2- *"Significant positive correlations were found, respectively, between TOM content and P16 PAHs concentration (r = 0.595, P < 0.01)"* (**Wang** et al., 2015)

Wang, Xiaowei, et al. "Characterizing the parent and oxygenated polycyclic aromatic hydrocarbons in mangrove sediments of Hong Kong." *Marine Pollution Bulletin* 98.1-2 (2015): 335-340.

3- During the research 16 PAHs (selected as priority PAHs by the EU and the USEPA) are measured. The candidate proposes additional research to develop analytical methods and toxicological information for other non-priority PAHs. Do you have any suggestion for which non-priority PAHs the analytical methods and toxicological information should be extended?

Response

Thank you very much for this insightful and valuable question. Yes, there are non-priority PAH compounds for which analytical methods and toxicological information should be further developed and expanded.

The non-priority PAHs including 5-methylchrysene (5-MC), 7,12-dimethylbenz[a]anthracene (7,12-DMBA), benz[j]aceanthrylene (B[j]A), cyclopenta[cd]pyrene (CPP),, anthanthrene (ANT), dibenzo[ae]pyrene (Db[ae]P), and Db[al]P have been reported to cause mutagenic effects and have been being associated with a risk of carcinogenicity. Retene (RET) and benzo[c]fluorine (B[c]F) showed evidence of a strong influence on the mutagenicity and carcinogenicity endpoints.

These compounds may have serious effects on human health because of their genotoxic, mutagenic, and carcinogenic potential in different experimental models. Certainly, more studies are needed to better understand the effects of non-priority PAHs on human health.

References

da Silva Junior, Francisco Carlos, et al. "A look beyond the priority: A systematic review of the genotoxic, mutagenic, and carcinogenic endpoints of non-priority PAHs." *Environmental Pollution* 278 (2021): 116838.

Sincerely

Ruqayah Grmasha

Ruqayah Ali Naser Grmasha

2/6/2025