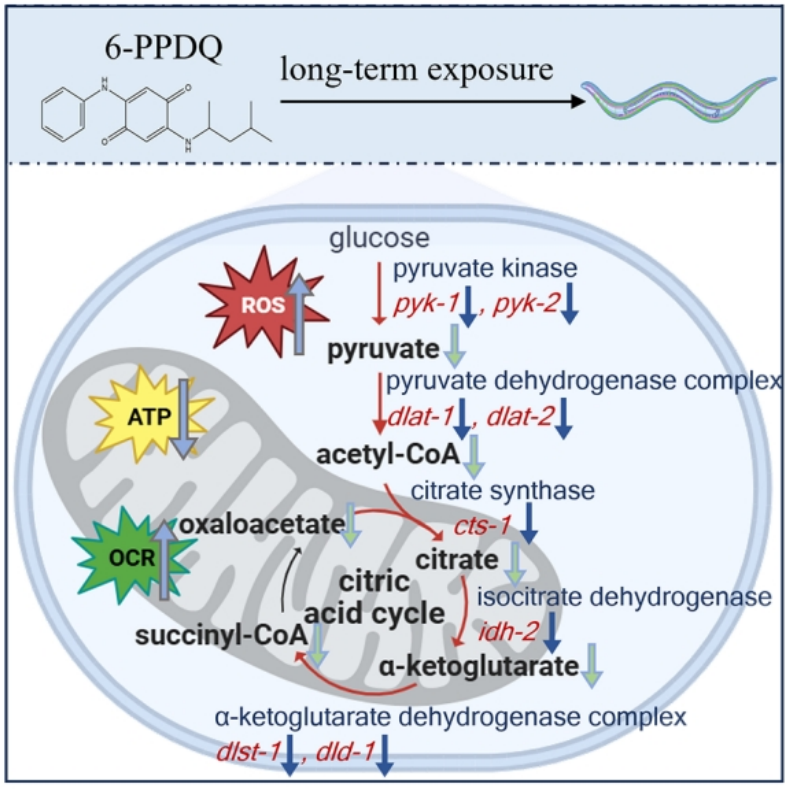
6-PPDQ disrupts citric acid cycle in C. elegans via reduced acetyl CoA and pyruvate

FAYETTEVILLE, GA, UNITED STATES, July 2, 2025 /EINPresswire.com/ -- Researchers explore how 6-PPD quinone (6-PPDQ), an environmental contaminant derived from tire antioxidant N-(1,3-dimethylbutyl)-N'-phenyl-p-phenylenediamine (6PPD), affects the citric acid cycle in C. elegans at environmentally relevant concentrations. The research reveals significant reduction in the citric acid cycle intermediates and key enzyme gene expressions by 6-PPDQ exposure, highlighting the its potential exposure risk on citric acid cycle metabolism.



HOW Does 6-PPDQ disrupts the citric acid cycle in caenorhabditis elegans.

6-PPDQ, has emerged as an environmental concern due to its widespread detection and toxic effects. In a study published in Environmental Chemistry and Ecotoxicology, researchers from Southeast University in China explored the effects of 6-PPDQ on the citric acid cycle and underlying mechanism in C. elegans. The citric acid cycle, a crucial metabolic pathway occurring in the mitochondria, plays a central role in cellular metabolism by linking carbohydrate, fat, and amino acid metabolisms. It provides intermediates for the synthesis of amino acids, fatty acids, and glycogen, which are essential for sustaining life activities.

The study reveals how 6-PPDQ at environmentally relevant concentrations (0.1–10 μg/L) disrupted the citric acid cycle by reducing intermediate metabolites, including citric acid, α-ketoglutarate, succinate, fumarate, malate, and oxaloacetate. Additionally, the reduction of these intermediate metabolites was due to the inhibition of relevant key enzyme gene expressions. Exposure to 6-PPDQ suppressed genes encoding citrate synthase (cts-1), isocitrate dehydrogenase 2 (idh-2), and α-ketoglutarate dehydrogenase complex (dlst-1, dld-1). As

explained by the researchers, “exposure to 6-PPDQ significantly impacts the citric acid cycle in C. elegans, which is crucial for understanding the potential risks of this contaminant to both environmental and human health.”

The researchers also observed that 6-PPDQ exposure decreased acetyl CoA and pyruvate contents, which are important for the control of citric acid cycle. Acetyl CoA generated from pyruvate is a key substrate for the cycle. The study found that among the genes encoding components of the pyruvate dehydrogenase complex, which controls acetyl CoA synthesis, only dlat-1 and dld-1 expressions were decreased by 6-PPDQ. The expressions of genes pyk-1 and pyk-2 associated with pyruvate generation were also reduced. RNA interference (RNAi) of these genes further exacerbated the cycle's disruption, highlighting the crucial contribution of these alterations to 6-PPDQ-induced toxicity.

The study also demonstrated that the disruption in citric acid cycle and reduction in acetyl CoA and pyruvate contents contributed to mitochondrial dysfunction, as indicated by increased oxygen consumption rates and decreased ATP content in 6-PPDQ exposed nematodes. Furthermore, the researchers investigated the protective effects of sodium pyruvate treatment, finding that it could suppress toxic effects of 6-PPDQ. “Our results suggest that sodium pyruvate treatment may be a promising approach to against 6-PPDQ toxicity,” the researchers concluded.

This study provides valuable insights into the mechanisms by which 6-PPDQ disrupts metabolic process of citric acid cycle and highlights the potential risks of this contaminant. The findings underscore the importance of further research to fully understand the implications of 6-PPDQ exposure for both environmental and human health.

References
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