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Polyethylene glycol used as a dispersant potentiates the toxicity of insecticides in mammalian cells rather than insects

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ABSTRACT

Insecticides are used in household products with various dispersants such as polyethylene glycol (PEG) and polyoxyethylene lauryl ether (PLE) to improve solubility. Although certain effects are expected, the combination effects of insecticides and dispersants remain elusive. Here, five different classes of insecticides (i.e., dinotefuran, fipronil, hydramethylnon, indoxacarb, and etofenprox) were dispersed in water, PEG, and PLE, and their lung inflammation potential was evaluated by bronchoalveolar lavage fluid analysis 24 h after intratracheal instillation into the lungs of rats. All chemicals dispersed in water caused no inflammation. However, among the five chemicals dispersed in PEG and PLE, only hydramethylnon showed significant neutrophilic inflammation and hydramethylnon in PEG showed 4-fold higher inflammogenic potential than that in PLE. The *in vitro* cytotoxic potential of hydramethylnon in PEG was 10–17 fold (in A549) or 12–14 fold (in dTHP-1) higher than that of hydramethylnon in PLE, and greater than 370 fold (in A549) or 65–169 fold (in dTHP-1) higher than that in water. PEG toxicity increased due to the micellar formulation of hydramethylnon in PEG, increasing cellular uptake by simple diffusion. Therefore, the observed potentiation effect highlights that the combination effect of formulation of hydrophobic compounds with dispersants should be carefully evaluated.

1. Introduction

Insecticides control insects in the agricultural, industrial, and domestic sectors to improve crop yields and quality of life. They are available as sprays, baits, dust, and gels, and their household usage has rapidly increased (Stejskal et al. 2021). Although insecticides are designed to benefit humans by protecting against various insect-spread diseases in crops, animals, and humans, their overuse in multiple fields can harm many species and damage ecosystems (Rezende-Teixeira et al. 2022; Yadav 2010). Furthermore, improper knowledge, poor storage, and excessive use of household chemicals contribute to indoor exposure and cause health risks (Sarwar 2016). Indoor air pollution from various sources including pesticides and volatile organic compounds is one of the greatest threats to public health, and upper-bound risks are much greater than the health risks associated with most other environmental problems (Wallace 1991). Furthermore, the tragic incidents related to humidifier disinfectants in South Korea warn regarding the safety of household chemicals, particularly inhalation exposure routes (Kim et al. 2014). The use of insecticides has exponentially increased owing to the coronavirus disease 2019 (COVID-19) pandemic (Choi et al. 2024) and the recent endemic outbreaks of bed bugs (Cimicidae), which have caused public concerns (Hasnaoui et al. 2023) not only about the effects of insects and pathogenic agents on human health, but also about resistance to insecticides in target organisms (Lewis et al. 2023).

Abbreviations: PEG, polyethylene glycol; PLE, polyoxyethylene lauryl ether; BALF, bronchoalveolar lavage fluid; MTS, 3-(4,5-dimethylthiazol-2-yl)-5-(3-carboxymethoxyphenyl)-2-(4-sulfophenyl)–2H-tetrazolium; LDH, lactate dehydrogenase; MIP-1β, macrophage inflammatory protein-beta; IL, interleukin; TNF-α, tumor necrosis factor; SD, standard deviation; PBS, phosphate-buffered saline; DW, distilled water; FBS, fetal bovine serum; dTHP-1, differentiated THP-1; DMEM, Dulbecco's Modified Eagle's Medium; RPMI-1640, Roswell Park Memorial Institute 1640; EC, effective concentration.

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