Toxicological Evaluation of Vape Liquids Circulating in Brazil: Evidence of Emerging Hazards

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Introduction: The increasing recreational use of electronic cigarettes has emerged as a pressing public health concern, with a growing body of evidence linking these products to significant toxicological risks. Over the past 25 years, numerous studies have identified hazardous chemicals in e-cigarette aerosols and liquids, underscoring their potential to cause serious harm. In Brazil, the sale of e-cigarettes is prohibited but their use continues to rise. **Objective**: This study aims to evaluate the cytotoxic and oxidative effects of e-liquids available in Brazil, analyzing how variations in origin and chemical composition influence their toxicological profiles. **Material**: E-liquids used in this study were donated by users and categorized based on their origin: Brazil (BR), China (CN), Europe (GB), the United States (US), and Paraguay (PY). **Methods**: Toxicity assessments were rigorously conducted using *Saccharomyces cerevisiae* to construct a growth inhibition curve, and regression analysis was employed to calculate the cytotoxic concentration that inhibits 50 % of the population. Subsequently, a spot test was performed to determine whether the effect on yeast growth occurred through a growth inhibition pathway or a lethal pathway. Additionally, cell viability assays were performed on rat cardiomyocytes while oxidative stress was assessed through the measurement of reactive oxygen species (ROS), catalase enzyme activity, and lactate dehydrogenase (LDH) integrity assays. **Results**: Our results demonstrate that the toxicity of e-liquids increases proportionally with concentration across all samples and groups. The cytotoxic concentration required to reduce cell viability by 50 % (CC_{50}) ranged from 3.8 % m/v for the Paraguayan sample to 20.4 % m/v for the European sample. Some e-liquids induced non-lethal inhibitory effects, while others triggered lethal cytotoxic pathways on yeast at higher concentrations. Samples from Brazil and Paraguay primarily followed a lethal growth inhibition profile on yeast, whereas samples from other regions exhibited non-lethal effects under similar exposure conditions. Mitochondrial activity-based cell viability significantly declined at concentrations above 0.625% m/v for several e-liquids. Additionally, oxidative stress markers, including reactive oxygen species (ROS) production, catalase activity, and lactate dehydrogenase (LDH) integrity, were altered for all samples. Certain e-liquids from the U.S. and Brazil caused minimal oxidative stress while maintaining cell viability above 50%, whereas others, especially from China and Paraguay, induced stronger oxidative responses and cytotoxicity. Variations in flavor composition, VG/PG ratio, nicotine content, and geographic origin affect physicochemical properties like crystallization and stability, influencing toxicity. Brazilian, European, and Paraguayan samples showed lethal effects on yeast, with Brazil and Europe presenting the highest cytotoxic potential. In contrast, U.S. and Chinese samples mostly caused non-lethal inhibition, though some U.S. products contained crystallized additives that increased toxicity. Mitochondrial activity declined across all samples, particularly those with high additive concentrations. The GB sample, with oxidized nicotine and complex flavorings, showed the highest oxidative stress. **Conclusion**: Nicotine-free e-liquids still impaired cell function significantly. The results indicate that different e-liquids exhibit distinct toxicity profiles, influenced primarily by their concentrations and chemical compositions, regardless of their country of origin. E-liquid samples from countries with approved manufacturing standards and regulatory controls also demonstrated toxic effects. These findings highlight the need for new studies in order to protect public health.