

## **Effects of electronic cigarette vapors exposure on oxidative damage and antioxidant status.**

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Electronic cigarettes (e-cigs) are devices designed to deliver nicotine without burning tobacco and therefore, they are perceived as a safer alternative to the conventional cigarettes. However, because of the high temperature reached by e-cig solutions (> 200 C°) many toxic substances, including polycyclic aromatic hydrocarbons, formaldehyde, nitrosamines, metals and carbonyls can be generated. Very few in vivo animal studies have been conducted so far, most of them based on short-term e-cig exposure.

The aim of this study was therefore to evaluate the influence of e-cigs on oxidative stress related parameters, classical markers associated to conventional cigarette toxicity.

Male Sprague Dawley rats (8 weeks of age), were housed in an inhalation chamber and exposed either to e- cig vapors (1 mL/day of e-liquid containing 18 mg/mL of nicotine) or to a saline solution. One cycle of treatment consisted in 17 sec puff, 6 sec on, 5 sec off, 6 sec on, followed by 20 minutes stop. e-cigs voltage was set at 5.5. Animals were submitted to 11 cycles/ day for 5 consecutive days/week, for 4 consecutive weeks. At sacrifice, liver, kidneys, lungs, bladder and plasma were collected for the analysis of protein (carbonyl residues) and DNA oxidative damage (8-hydroxy-2'-deoxyguanosine (8-OHdG)) and of the total antioxidant power (FRAP assay).

At lung level, we found that FRAP values of rats exposed to e-cigs vapors were markedly reduced compared to controls. A similar trend was observed in the plasma, even if the statistical significance was not reached. Plasma FRAP levels and carbonyl residues were inversely correlated in e-cig exposed rats but not in controls. We also found that 8-OHdG markedly increased in the lung of e-cig vapor exposed rats compared to controls. An inverse correlation between FRAP levels and 8-OHdG in lung tissue from exposed animals was also observed.

These results demonstrate that e-cig vapor causes DNA oxidative damage and impairs antioxidant defenses in rats; given that these toxicological outcomes are typically induced by conventional cigarettes smoking, further investigations to better identify harmful e-cig effects especially in the long term, are of paramount importance.