ASSESSING THE ROLE OF SUPRA-PHYSIOLOGIC LEVELS OF RETINOIDS IN OVALBUMIN-SENSITIZED LUNG TISSUE AND REVERSAL OF RELATED PATHOLOGY BY CITRAL IN THE FISCHER RAT MODEL

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Abstract: The role of retinoids (All Trans Retinoic Acid; ATRA, and Retinyl Palmitate; RP) in the development of lung hypervitaminosis A pathology is not well understood or established in the literature. As well, the role of citral (inhibitor of retinoid function) in the reversal of lung pathology is also not ascertained under an in vivo setting. Therefore, it is hypothesized that ovalbumin exposure will sensitize lung tissues to supra-physiologic levels of retinoids leading to tissue pathology and that citral 1 and 2 will reverse or ameliorate the related pathological damage to lung tissues. Even though ovalbumin and retinoids have been previously applied through intratracheal route in cancer prevention and immunological research, the objective of this pilot study was to evaluate techniques, establish functional dosing and generate preliminary data before further experimentation. This IACUC approved in vivo study consist of twenty (n = 20) Fischer 344 rats (200 to 400g) which were randomly assigned to controls and two treatment groups (low and high; all ovalbumin sensitized) and dosed at day 7 with 40 and 80 mg/kg ATRA and RP as well as 20 and 50 mg/kg of citrals 1 and 2 by intraperitoneal injection). Citral is a non-toxic chemical that exists in two forms (diethyl; C1 or cis-trans dimethyl; C2). Positive and negative controls for each treatment were also included in the study. Animals were housed in rat cages at the JSU Research Animal Core Facilities and were placed on a 12:12 light–dark cycle. A standard rodent diet and water access were provided ad libidum. All treatment animals were challenged with ovalbumin through intratracheal instillation on Day 7. Rat weights were recorded on Day 1 and 21, all animals were sacrificed on day 21 and lung tissues were processed for histopathology. Slides were prepared and were histopathologically digitized for comparison of tissues pathology status of the various treatments. Results showed that even though C1 and C2 were not toxic individually, their combination at high dosing was lethal. The combination of high dosing of RP and C1 was also lethal. Exposure of ovalbumin-sensitized rats to ATRA showed various levels of lung tissue damage that was ameliorated by C1. RP exposure caused various levels of tissue damage that was not reversed by either C1 or C2. On the other hand C2 did not reverse the damage caused by ATRA. Taken together, the study showed that there are variable responses for the interaction of citrals and retinoids in reversing tissue pathologies and that these findings warrants further investigation as to the actual role of these interactions as related to chronic lung disease and the reversal of retinoid-related pathologies in the Fisher rat model.

Key words: ATRA, RP, Citral, F344, Ovalbumin, Chronic Lung Pathology, Hypervitaminosis A

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