VEHICLE-DEPENDENT DISPOSITION KINETICS OF FLUORANTHENE IN FISHER-344 RATS

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Abstract: Fluoranthene [FLA] is member of the family of Polycyclic Aromatic Hydrocarbon chemicals. Fluoranthene exposure to humans may occur as a result of cigarette smoking, consumption of contaminated food and water, heating woods in stoves and boilers, industrial sources such as coal gasification, carbon and graphite electrode manufacturing. Of all these sources, ingestion of contaminated food serves as the major portal of entry for FLA. In oral toxicity studies using animal models, the vehicles used to deliver the toxicants may influence the systemic absorption, metabolism and clearance from the body. The objective of this study was to evaluate how the vehicles of choice affect the pharmacokinetics of orally administered FLA in rats. Adult male Fisher-344 rats were given single oral doses of 25 and 50 µg/kg FLA in tricaprylin, peanut oil, cod liver oil and 10% Alkamuls-EL620 through gavage. Soon after administration, the rats were housed individually in metabolic cages and sacrificed at 2, 4, 6, 8, 12 and 24 hours post FLA exposure. Blood, lung, liver, small intestine, adipose tissue samples, urine, and feces were collected at each time point. Samples were subjected to a liquid-liquid extraction using methanol, chloroform, and water. The extracts were analyzed by a reverse-phase HPLC, equipped with a fluorescence detector. A dose-dependent increase in FLA concentrations was noted in plasma and tissues for all the vehicles used. Plasma and tissue FLA concentrations were greater for peanut oil; cod liver oil, and tricaprylin vehicles compared to Alkamuls (p < 0.05). Most of the FLA administered through peanut oil, cod liver oil and tricaprylin was cleared from the body by 8 hours (90%) and 12 hours (80%) post administration for the 25 µg/kg and 50 µg/kg dose groups, respectively. However, when FLA was administered through Alkamuls, at the end of 12 hours, only 60% of the FLA was cleared from the body in the 25 µg/kg group and 40% in the 50 µg/kg group. These findings suggest that uptake and elimination of FLA is accelerated when administered through oil-based vehicles. The low uptake of FLA from Alkamuls may have been a result of the poor solubility of the chemical. In summary, our findings reiterate that absorption characteristics of FLA were governed by the dose as well as the dosing vehicle. The vehicle-dependent bioavailability of FLA calls the need for judicious selection of vehicles in evaluating oral toxicity studies for risk assessment purposes.

Keywords: Fluoranthene, pharmacokinetics, absorption, tricaprylin, peanut oil, cod liver oil, and Alkamuls.

Acknowledgements: This research was supported in part by the National Institutes of Health grants, ES012168 (AR), S11ES014156-01 (DBH & AR), NS41070 (DBH), 5T32HL007735-12 (DLH), and G12RRO3032 (Meharry).