Bethany R Baumgart, J Clinic Toxicol 2016, 6:5(Suppl)
http://dx.doi.org/10.4172/2161-0495.C1.018

D-α-tocopheryl polyethylene glycol 1000 succinate (TPGS)-containing vehicles provide no detectable chemoprotection from oxidative damage

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Pharmaceutical formulations (vehicles) used to administer test articles to animals often contain excipients to enhance delivery of the test compound. The common excipient d-α-tocopheryl polyethylene glycol 1000 succinate (TPGS) increases solubility and maximizes systemic exposure of lipophilic test articles. Given the well established antioxidant properties of d-α-tocopheryl succinate (TS), a component of TPGS, and d-α-tocopherol (TOC), hydrolyzed TS, we examined the potential protective effects of vehicles containing TPGS. Such effects could mask potential toxicities of test articles, including processes involved in carcinogenesis, and impact nonclinical safety assessments. Male and female Sprague-Dawley rats were administered vehicles containing 5% or 40% TPGS (70 or 550 mg/kg/day TS, respectively) orally for 1 week. A control group was administered polyethylene glycol-400 (PEG-400; no vitamin E) orally and positive control animals received a single 100 mg/kg intraperitoneal (IP) injection of TS. Additionally, whole blood from untreated animals was incubated with 5 or 50mM H_2O_2 *ex vivo* with or without TS (0.5, 5, 50, or 500μM) or ascorbate (1mM), as a positive control, for 1 hour. Plasma, liver, and adrenal gland concentrations of TS and TOC as well as oxidative status of plasma were evaluated following oral administration of TPGS-containing vehicles, IP injection of TS, or treatment of whole blood with H_2O_2 *ex vivo*. Oral TPGS administration did not affect TOC concentrations in plasma or adrenal glands and caused only transient increases in liver. Concentrations of TS in plasma, liver, and adrenal glands were undetectable in control animals, but increased with administration of vehicles containing 5 and 40% TPGS. Oral administration of TPGS did not reduce plasma lipid peroxidation *in vivo*. Substantially greater TS concentrations (100× greater than *in vivo*) added to H_2O_2-treated whole blood *ex vivo* were also unable to reduce lipid peroxidation. These results provide evidence that administration of oral TPGS vehicles is unlikely to impact nonclinical carcinogenicity safety assessments of pharmaceuticals.

Biography

Bethany R Baumgart completed her Bachelor of Science degree in Biology in 2009 and Master of Science degree in Biology and Biotechnology in 2011, both from Ball State University. She is a Research Scientist I in Toxicology at Bristol-Myers Squibb Company with roles as a member of the Molecular and *In Vitro* Toxicology Laboratory as well as nonclinical study director.

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