Dibutylphthalate Pharmacokinetics in Pregnant Rats

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Gestational and lactational exposure of rats to di(n-butyl)phthalate (DBP) results in malformations of the male reproductive tract. Since these effects are observed at high exposure concentrations (250-750 mg/kg/day), saturation of metabolism may contribute to the generation of effects and may be an important consideration in a risk assessment for this chemical. The objective of this project is to examine the kinetics of DBP in pregnant rats at gestation day (gd) 20 at three dose levels. The distribution of DBP, monobutylphthalate (MBP), and its glucuronide metabolite in plasma and maternal tissues will be determined. A pilot study has been conducted in which the metabolism of 14C DBP has been examined in the female rat. The major urinary metabolites were MBP and MBP glucuronide. A standard of MBP glucuronide has been prepared. In a second pilot study, 14C DBP was administered to pregnant rats on gd 20, and the metabolites in plasma were identified by high performance liquid chromatography (HPLC). The samples obtained are being used in the development of methods for analysis of DBP, MBP, and its glucuronide in plasma. Transfer of DBP, MBP, and its glucuronide metabolite across the placenta in pregnant rats will be evaluated at several dose levels. This project will continue (under the direction of Dr. Susan Borghoff) as part of CIIT’s ongoing antiandrogen program project.

Start and end date: January 2000 – December 2002.

Presentation(s):


Peer-reviewed publication(s):


Other publication(s): None to date.

Sponsors in addition to the LRI: None.

Abstract revision date: January 2006.