MEDIUM CHAIN CHLORINATED PARAFFIN (MCCP)-INDUCED HAEMORRHAGIC LESIONS IN NEONATAL SPRAGUE-DAWLEY RATS. A ROLE FOR ALTERED VITAMIN K DISPOSITION?

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Introduction
A previous study with MCCPs administered to female rats prior to pregnancy and during gestation indicated increased pup mortality; that was associated with internal haemorrhages. This study was designed to provide more data to elucidate the mechanism of the internal haemorrhaging, thus assisting hazard identification and risk assessment. The hypothesis tested was that MCCPs interfered with blood clotting due to modulation of Vitamin K disposition.

Experimental

Study Design
- The study was designed to provide samples throughout the lactation period, but because of an unacceptable increase in pup mortality in the Test Group animals, the study was terminated prematurely approximately 2 weeks after the first litters were born.
- Treated rats received a constant concentration of 6250 ppm MCCP in the diet for 4 weeks prior to pairing, then throughout the mating, gestation and lactation periods. Control animals received untreated diet (Figure 1).

Results
- Vitamin K concentrations in milk were markedly decreased by MCCPs (Table 2).
- MCCP concentrations in milk were 981 ± 325 µg/mL (n=3) and 24423 ± 8151 µg/mL (n=9) at day 1 and day 12 of lactation respectively.
- On Day 1 of lactation, liver weights were marginally increased in MCCP Group pups. At Day 4 pup liver weights in the MCCP Group were significantly greater than the Controls (data not shown).
- Pup plasma volumes were insufficient to measure vitamin K directly, however, it was possible to use clotting factor activities as surrogates. MCCP treatment led to decreased factor VII and X activities (Table 2).

Discussion
The marked decrease in the maternal plasma concentration of vitamin K was reflected by decreased vitamin K levels in the milk. Vitamin K is obtained from the diet and from gut microflora. Neonatal animals have a sterile gut and depend on the vitamin K content of their mother’s milk. In the case of decreased supplies of vitamin K (eg. none during days 1-4 post-partum) haemorrhagic lesions are likely to occur.

MCCP treatment, leading to decreased activity of clotting factors VII and X (Table 2). Prothrombin times in the dams were unaffected (data not shown). The study was designed to provide samples throughout the lactation period, but because of an unacceptable increase in pup mortality in the Test Group animals, the study was terminated prematurely approximately 2 weeks after the first litters were born.

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