Pharmacokinetics of the Phytoestrogen Genistein During Pregnancy and Lactation

Susan Borghoff, Principal Investigator
Nicole Soucy, Coinvestigator, postdoctoral fellow
CIIT Centers for Health Research.

Genistein is a phytoestrogen that occurs in commercial rodent diets and has been reported to bind to estrogen receptors in vitro and elicit estrogenic effects in developing rodents. The differentiating reproductive organs of embryos, fetuses and newborns are considered to be particularly sensitive to hormonally active chemicals. Thus upon indirect pre- and early postnatal exposure through a pregnant or lactating animal fed with a commercial diet containing phytoestrogens, the offspring may be at risk for estrogenic actions of a chemical such as genistein. There is very little information available on the dosimetry of genistein in target tissues that contain estrogen receptors or about the transplacental or lactational transfer of this compound. Many of the studies have focused on measuring total genistein following hydrolysis of conjugated genistein metabolites. This research program has been directed towards 1) evaluating the pharmacokinetics of genistein in nonpregnant rats to develop methods to quantitate both parent and major conjugated metabolites in tissues, 2) evaluating the ability of selected genistein and its major metabolites to interact with the estrogen receptors to determine their potential for these metabolites to contribute to any estrogenic responses associated with genistein exposure and, 3) pharmacokinetics of genistein in pregnant rats following single and repeated administration to determine the extent and rate of placenta transfer of genistein and metabolites to the developing fetus. The outcome of these investigations have provided critical data that is being used to refine and verify a physiologically based pharmacokinetic model to describe the distribution of genistein to target tissues with high levels of estrogen receptors in both nonpregnant and pregnant rats. Emphasis this year will be towards completion of a repeated pharmacokinetic study in pregnant rats and investigating the significance high genistein concentrations in the placenta has on fetal development. Quantitative determinations of the relationship between target tissue concentrations and biological activity will provide insights as to the potential risk from exposure to genistein in the diet.


Presentation(s):


This abstract was prepared by the principal investigator for the project. Please see www.USLRI.org for more information about the LRI.


Peer-reviewed publication(s): None to date.

Other publication(s):


Additional sponsors: None.

Revision date: February 2005.