Genistein Study (phytoestrogen)

Lab: Syngenta[1]

Groups of fifteen male Alpk:APfSD (Wistar-derived) rats were dosed orally by gavage with 0, 50, 120, 400 or 1000 mg Genistein/kg/day for 15 consecutive days. Clinical observations, bodyweights and food consumption were measured throughout the study. At the end of the scheduled period, the animals were killed and necropsied. Cardiac blood samples were taken for hormonal analyses, selected organs were weighed and specified tissues were taken for subsequent histopathological examination.

There was no effect of Genistein administration on clinical signs, organ weights or on the findings observed at necropsy, either macroscopically or by microscopic evaluation. No changes were observed in hormone levels that could conclusively be attributed to Genistein administration.

Administration of Genistein to male rats at a dose level of 1000 mg/kg/day for fifteen consecutive days resulted in lower bodyweights and food consumption. There were no changes in the hormone levels or other parameters measured that could definitively be attributed to Genistein administration. There were no changes observed for the males in the groups dosed at 50, 120 or 400 mg/kg/day that could definitively be attributed to Genistein administration.

[1] For more details of this study, contact Rick_Becker@americanchemistry.com

Methyltestosterone Study (androgen agonist)

Lab: WIL[1]

Methyltestosterone in the vehicle, 0.25% aqueous methylcellulose, was administered orally by gavage once daily for 16 consecutive days to five groups of 15 male Crl:CD®(SD)IGS BR rats. Dosage levels were 0, 10, 30, 100 and 300 mg/kg/day, and the dose volume was 5 mL/kg/day for all groups.

All animals were observed twice daily for mortality and moribundity. Clinical examinations were performed daily. Individual body weights and food consumption were recorded daily. Clinical pathology evaluations (hormone analysis) were performed on all animals on the day of necropsy. All animals were euthanized on study day 16. Complete necropsies were conducted on all animals, and selected organs were weighed and specific organs were examined microscopically.

There were no test article-related deaths. The clinical condition of the animals in the 10, 30 and 100 mg/kg/day groups was unaffected by test article administration. No test article-related changes in T_3, T_4, estradiol, TSH and DHT levels or in thyroid and epididymal weights were observed. No test article-related macroscopic changes were observed at necropsy. No test article-related changes were noted in the 10 mg/kg/day group. The following substance related findings were reported:

300 mg/kg/day group:

- Mean body weight losses and reduced body weight gains, food consumption and food efficiency (statistically significant).
- Decreasing trends (stat. significant) in levels of testosterone, LH and FSH.
- Increasing trend (statistically significant) in prolactin levels.
- Decreased (statistically significant) mean absolute testis weight.
- Increased (stat. significant) mean liver weight relative to body weight.
- Increased mean absolute weight of accessory sex gland unit, seminal vesicles and prostate (usually statistically significant).
- Microscopic changes in the testes (mild to moderate interstitial cell atrophy) in 15/15 males.

100 mg/kg/day group:

- Slight (not statistically significant) mean body weight losses and reduced body weight gains, food consumption and food efficiency.
- Decreasing trends (stat. significant) in testosterone, LF and FSH levels.
- Microscopic changes in testes (min. to mild interstitial cell atrophy) in 12/15 males.

30 mg/kg/day group:

- Decreasing trends (statistically significant) in testosterone and luteinizing hormone.

Conclusion: Oral administration of methyltestosterone to intact male rats for 16 consecutive days produced changes in serum hormone levels, organ weights and microscopic changes to the testes. These results from oral administration are similar to those observed by IP administration of testosterone reported by other investigators.

[1] For more details of this study, contact Rick_Becker@americanchemistry.com

p-Nonylphenol Study (estrogen receptor agonist (weak or partial))

Lab: BASF[1]

Para-Nonylphenol was administered to groups of 15 male Wistar rats by gavage for 14 consecutive days at doses of 0 (vehicle control), 5, 20, 80 and 200 mg/kg body weight/day. Food consumption was determined weekly and body weight measured daily. Animals were examined for clinical signs of toxicity at least once daily.

At study termination, blood was collected for hormone measurements. All animals were subjected to necropsy and histopathological evaluation of selected tissues.

The following substance related findings were reported:

200 mg/kg bw/day Dose Group

- Abnormal clinical signs in several animals
- Reduced food consumption, body weights and food efficiency
- Decreased testosterone and estradiol levels
- Decreased mean absolute and relative weights of accessory sex organs
- Increased mean relative liver weight
- Centrolobular hepatic hypertrophy in most animals
- Diffuse follicular cell hyperplasia in thyroid glands in individual animals
- Multiple focal degeneration of seminiferous epithelium in tests in some animals

80 mg/kg bw/day Dose Group

- Abnormal clinical signs in one animal
- Decreased testosterone and estradiol levels
- Increased mean relative liver weight

20 mg/kg bw/day Dose Group

- Increased mean relative liver weight

5 mg/kg bw/day Dose Group

- No Substance related effects

In conclusion, administration of para-nonylphenol in the Intact Male Assay caused weight changes in the accessory sex organs and decreases in serum testosterone and estradiol levels in the highest dose group (200 mg/kg bw/day). Liver weight was increased and histopathological changes were seen in liver, thyroid and testes. Similar effects on hormone levels and liver pathology were seen in the 80 mg/kg dose group.

[1] For more details of this study, contact Rick_Becker@americanchemistry.com