Uterotrophic bioassay in immature rats

A MODEL FOR THE TESTING AND ASSESSMENT OF ENDOCRINE DISRUPTING CHEMICALS

Model

The uterotrophic assay is a bioassay for oestrogenicity testing to identify substances with the potential to interact with the endocrine system, ultimately leading to risk assessments for human health or the environment. It is based on the measure of the increase of uterine weight.

Oestrogen agonists and antagonists act as ligands for oestrogen receptors α and β and may have the potential to lead to adverse health hazards, including reproductive and developmental effects. Therefore, the need exists to rapidly assess and evaluate a chemical as a possible oestrogen agonist or antagonist. Uterine tissues respond with rapid and vigorous growth to stimulation by oestrogens, particularly in laboratory rodents, where the oestrous cycle lasts approximately 4 days. The Uterotrophic Bioassay relies for its sensitivity on an animal test system into which, the hypothalamic-pituitary-ovarian axis is not functional (e.g. immature female rat), leading to low endogenous levels of circulating oestrogens. This will ensure low baseline uterine weights and a maximum range of response.

Specie

Rat

Interest

- This model is available in rats as the rat is the species of choice in most reproductive and developmental toxicity studies.
- The method uses immature non-ovariectomized rats, avoiding surgical pre-treatment of the animals.
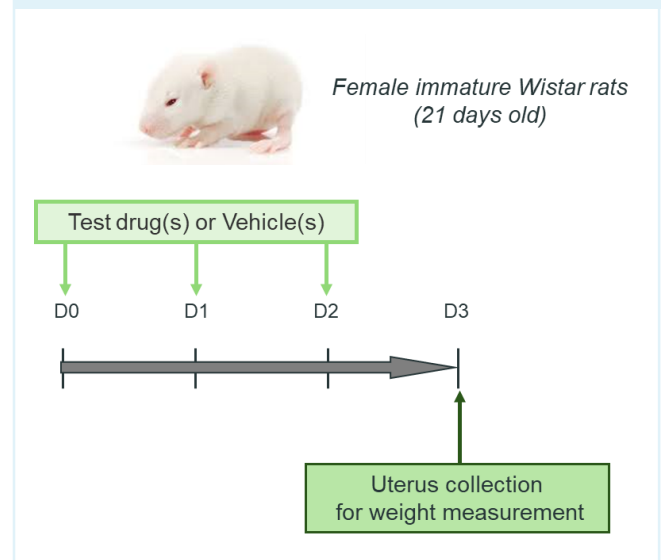
Model Description

- Female immature rats (21 days old) are used.
- Test substance is administered daily by oral gavage (to model ingestion) or subcutaneous injection (to model inhalation or dermal adsorption) for a minimum administration period of 3 consecutive days.
- General clinical observations are made at least once a day and rats are weighed daily.
- 1 day after the last dose, uterus is collected and weighed.
- Tissue samples (vagina…) can be collected for further histological analysis.

Parameter evaluated

Uterine weight (mg)

Example of protocol design

Female immature Wistar rats (21 days old)

Test drug(s) or Vehicle(s)

D0   D1   D2   D3

Uterus collection for weight measurement

Oestradiol and Tamoxifen boost uterotrophic effect whereas Fulvestrant exhibits anti-uterotrophic activity

- Vehicle 1 (s.c.)
- Fulvestrant (s.c.)
- Oestradiol (s.c.)
- Vehicle 2 (p.o.)
- Tamoxifen (p.o.)
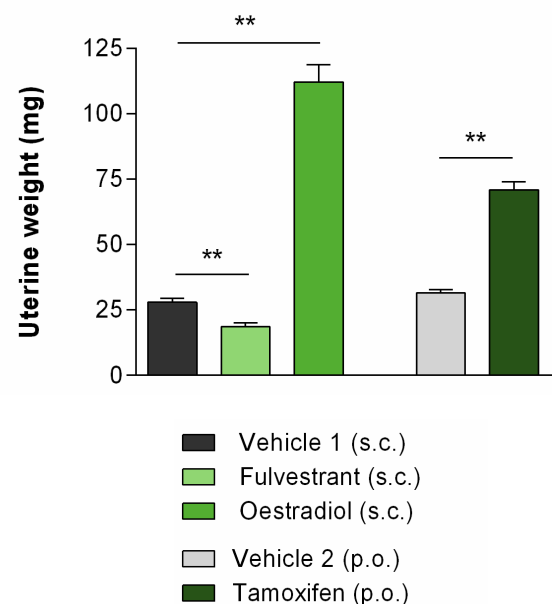
Oestradiol = oestrogen steroid hormone

Tamoxifen = oestrogen receptor modulator

Fulvestrant = selective oestrogen receptor degrader

**p<0.01 vs corresponding Vehicle. (n=5/group)