

EVALUATION OF REPRODUCTIVE TOXICITY ASSOCIATED WITH FIPRONIL EXPOSED FEMALE WISTER RATS

Project Reference No.: 47S_MSC_0014

College : Sharnbasva University, Kalaburagi

Branch : Department of Zoology

Guide(S) : Mr. Vishwajit Basavaraj Darekar
Dr. Basawarajeshawri Indur

Student(S) : Ms. Sadika Sumera
Mr. Naveenkumar Mallappa Sindagi
Mr. Sameer Panaparosh
Ms. Tanuja Hirole

Introduction:

Disorders of reproduction and hazards to reproductive health have become a prominent public health issue. Numerous agents including pesticides, plasticizers, metals and several industrial chemicals have been shown to cause reproductive toxicity in male and female laboratory animals and humans (Dalsenter et al., 1997, Faqi et al., 1998, Gray et al., 1999). For more than two decades in the world literature uses the term “endocrine- disrupting chemicals or endocrine disruptors” (EDCs, or EDs), adopted by the Agency for the U.S. Environmental Protection Agency in 1991 (Boas et al., 2006; Diamanti-Kandarakis *et al.*, 2009; Zoeller, 2010). This term brings together all chemical substances which in the humans and animals changing processes of synthesis , secretion, transport, and metabolism of natural hormones and thereby leads to a violation of hormonal homeostasis (Hotchkiss *et al.*, 2008). Endocrine-disrupting effects have many pesticides, including the latest generation, and household chemicals and some medicines. There are more than one hundred pesticides of which 80% are commonly used as insecticides and fungicides, have different endocrine disrupting effects (Mnif *et al*, 2011). One of the most common representatives of the pyrazole class pesticides is fipronil (FPN), which as insecticide has a high efficiency even at low doses and is widely used in households, agriculture, and health care in the many countries of world (Tingle et al., 2003). Fipronil is a second-generation phenylpyrazole insecticide widely used in veterinary medicine as well as a food-use pesticide. It is effective at low doses against numerous terrestrial insects, such as insect pests of crops and locusts. It has also excellent therapeutic and persistent activity against ticks and fleas when topically administered to domestic

animals. Fipronil is a potent inhibitor of the gamma-aminobutyric acid (GABA)-gated chloride channel and insect death is caused by hyper-excitation, convulsions and paralysis.

The purpose of the present study is to elucidate whether fipronil poses reproductive hazards in adult female Wistar rats acutely exposed by topical administration of a formulated product, since the area of kalaburagi district where framers used to practice fipronil regularly to control various pests in pulses, cotton and cereals will be exposed to this harmful insecticide. Hence this study will help to explore the effects of fipronil (FPN) on reproductive health of daily wage labours and farmers. A sufficient number of well-validated endpoints were investigated in order to provide a comprehensive risk assessment of the entire reproductive system.

Objectives

1. The effect of Fipronil on sexual behaviour and fertility in adult female rat
2. Developmental and Reproductive outcomes in female rats exposed to fipronil chemicals.

Methodology:

Material

Test chemical

Fipronil, White crystalline powder, Purchased from Tokyo Chemical Industry (TCI) India PVT LTD, Genome Valley Rd, Turkapally, Hyderabad, Telangana- 500078, India.

Animals

Female Wistar rats, approximately 10 weeks old obtain from Animal House, Department of P.G. Studies and Research in Zoology, Sharnbasva University Kalaburagi, Karnataka. The rats are acclimatized for five days before start of the treatment. The animal experiment will perform in accordance with the guideline for care and use of laboratory animals. All experimental protocols were approved by the Institutional Animal Ethics Committee. IAEC Approval no: (SUK/ZOL/IAEC/05/2024-

25) of Department of P.G. Studies and Research in Zoology, Sharnbasva University Kalaburagi, Karnataka, India (CPCSEA Regd. no.: 2236/PO/ReBiBt/S/23/CCSEA).

Housing, bedding, diet and water

Rats were housed in an environment-controlled room (temperature: 21 ± 3 °C with relative humidity between 58 and 67%; 12 hours light and 12 hours dark cycle). The sterilized paper shreds were provided nesting material. Pelleted rodent feed (Champaka Feeds and Foods, Bangalore, India) and purified water in polycarbonate bottles were provided ad libitum.

Experimental Design and test doses

The rats were randomly divided into four groups, each group containing 10 rats. Administration duration of fipronil will chose according to the completion time of oogenesis and in accordance with the OECD Guideline for Testing of Chemicals: The doses of Fipronil were determined according to previous studies and also, the exposer of human have chosen were in accordance with the guidelines extrapolating human doses to animal doses

Female rats were divided into following groups:

Group 1 – (Control): The rats of this group received vehicle (distilled water) for 30 days.

Group 2 – Fipronil Low dose [10 mg/kg body by oral gavage 30 days]

Group 3 – Fipronil Medium dose [20 mg/kg body weight by oral gavage 30 days].

Group 4 – Fipronil high dose [30 mg/kg body weight by oral gavage 30 days].

After 24 hours of the last dose, the animals were weighed and autopsied under light ether anesthesia. The blood was collected through cardiac puncture using a dry and clean syringe, for serum studies.

Result And Conclusion:

The following reproductive parameters examination will be conduct at the end of the experiment:

1. Study of oestrous cycle length
2. Determination body and organ weight
3. Histological examination of Ovary tissue

4. Determination of serum FSH, LH, Estrogen levels
5. Analysis Serum Biochemistry
6. Statistical analysis

References:

1. Boas, M., Feldt-Rasmussen, U., Skakkebaek, N.E., Main, K.M., 2006. Environmental chemicals and thyroid function. *Eur. J. Endocrinol.* 154, 599–611.
2. Dalsenter, P.R., Faqi, A.S., Webb, J., Merker, H.J., Chahoud, I., 1997. Reproductive toxicity and toxicokinetics of lindane in the male offspring of rats exposed during lactation. *Hum. Exp. Toxicol.* 16, 146–153.
3. Faqi, A.S., Dalsenter, P.R., Merker, H.J., Chahoud, I., 1998. Reproductive toxicity and tissue concentrations of low doses of 2,3,7,8-tetrachlorodibenzo-p-dioxin in male offspring rats exposed throughout pregnancy and lactation. *Toxicol. Appl. Pharmacol.* 150, 383–392.
4. Hotchkiss, A.K., Rider, C.V., Blystone, C.R., Wilson, V.S., Hartig, P.C., Ankley, G.T., Foster, P.M., Gray, C.L., Gray, L.E., 2008.
5. Mnif, W., Hassine, A.I., Bouaziz, A., Bartegi, A., Thomas, O., Roig, B., 2011. Effect of endocrine disruptor pesticides: A review. *Int. J. Environ. Res. Public Health* 8 (6), 2265–2303.
6. Organisation for Economic Co-operation and Development. (1996). OECD Guideline for Testing of Chemicals. Combined Repeated Dose Toxicity Study with the Reproduction/Developmental Toxicity Screening Test, No. 422. OECD, France.
7. Tingle CCD, Rother JA, Dewhurst CF, Lauer S, KingWJ (2003) Fipronil: environmental fate, ecotoxicology and human health concerns. *Rev Environ Contam Toxicol* 176:1–66
8. Zoeller RT, Bansal R & Parris C. Bisphenol-A, an environmental contaminant that acts as a thyroid hormone receptor antagonist in vitro, increases serum thyroxine, and alters RC3/neurogranin expression in the developing rat brain. *Endocrinology* 2005 146 607–612.