MATERIALS AND METHODS
Clomiphene (Triarylethylene[p-(8-di-ethylaminoethoxy)-phenyl-1,2-diphenyl-2 chloroethylene]), a potent stimulator for induction of ovulation in anovulatory women, is known to behave as an estrogenic or antiestrogenic compound depending on the dosage used. It has also been shown to act as a potent postcoital antifertility agent in rats, mice, rabbits etc.

The antifertility property of clomiphene in rats has been previously proposed to be due to its blastotoxicity or zygototoxicity (Segal & Nelson, 1961; Davidson et al. 1965 a,b; Prasad et al. 1965), however, such a proposition has been nullified by Staples (1966) and Chatterjee et al. (1974).

Available literature suggests that chemically clomiphene is a mixture of its cis- and trans-isomers and it is proposed that the cis-form is much more potent compound to clomiphene or its trans-isomer. Experiments of the present dissertation have been designed to evaluate the antifertility faculty of clomiphene and its cis- as well as trans-isomers.

Animal preparation:

About three-month old rats of Wistar-derived strain were housed in a controlled environment and the lighting schedule maintained at 12 hr of light per day. The animals had free access to pelleted food and water. The animals used have shown at least three normal 4-day-cycle as determined by daily vaginal smears; animals with irregular cycles were discarded.

Pregnancy was produced by caging females on the evening of proestrus with males of proven fertility. The appearance of sperm in vaginal washings the following morning was considered evidence of positive mating and constituted day 1 of pregnancy.
Pseudopregnancy was induced by caging females on the evening of proestrus with vasectomized males. Decidual cell reaction (DCR) was induced by uterine traumatization on day 5 of pseudopregnancy as described by De Feo (1963).

Bilateral ovariectomy and hysterectomy were performed under light ether anesthesia via flank and mid-ventral incision, respectively.

At autopsy, the embryonic swellings and ovaries were dissected out and weighed on a torsion balance; the 4 largest corpora lutea (CL) from each group were microdissected and combined weight determined. The CL were taken from the same ovary and the establishment of 4 CL as the number weighed was a purely arbitrary choice. For histological assessment the remaining ovaries of each group were fixed in Bouin's fluid and processed accordingly.

Again, the traumatized and non-traumatized cornua were removed from the pseudopregnant rats on sacrifice, split at the bifurcation, the adhering tissues were trimmed off and each cornua weighed on a torsion balance and compared with the vehicle-injected controls.

**Chemicals used:**

Clomiphene citrate (Clomid), cis-clomiphene citrate and trans-clomiphene citrate were made available through the courtesy of Dr. K. W. Wheeler of N.M.S. Harrell Company, U.S.A. Reserpine (Serpasil®) was generously supplied by CIBA of India Ltd., Bombay. Progesterone (Proluton-Depot®) was obtained through German Remedies Private Ltd., India.
Treatment of animals:

Clomiphene citrate (clomid), cis-clomiphene citrate (cis-clomid) and trans-clomiphene citrate (trans-clomid) were dissolved in 0.9% saline and administered 3.0 mg/kg, 2 mg/kg and 10 mg/kg sc, respectively as per the schedule (Table 1).

Reserpine was used at a dose level of 0.5 mg/kg bw (Chatterjee & Harper, 1970) as per the treatment schedule (Table 2).

Progesterone (hydroxyprogesterone caproate) was diluted with corn oil was administered sc as a single daily injection in a volume of 0.2 ml of the vehicle as per the schedule (Tables 3 & 4).