INTRODUCTION
The pioneering work of Gregory Pincus in the late fifties on the use of progestational steroids for control of fertility ushered in a new era in the history of contraception. It has now become one of the very important methods for conception control and is widely practised by women around the world. Oral contraceptives, for the first time provided a method which is one hundred percent effective in controlling fertility if the "pill" is taken regularly according to the regimen. Over the years, the dose of the progestational steroid and the estrogen taken along with it have been reduced and small doses of progestins alone are also being used. Newer delivery systems for the administration of the progestational steroids are being explored. One such promising lead is the use of steroid-releasing implants.
A number of side effects have been encountered with the use of progestational steroids for the control of fertility. In the development of new formulations attempts have been made to reduce these side effects. However, except for minor improvements, there has not been much significant progress in this area. Furthermore, in spite of the enormous work, the mechanism of action of progestational steroids is not fully understood. Pincus (1957, 1965, 1966) suggested that the oral contraceptives act through the suppression of pituitary gonadotropins and thus inhibit ovulation. More recently, when new drugs and different dosages have been used, it has been recognised that these steroids have other sites of action and at times these may act at multiple sites giving evidence of their wide range effectiveness in controlling fertility. Suggestions of their action at the level of cervical mucus (Martinez-Manautou, Giner-Velasquez, Cortes Gallegos, Aznar, Rajo Guiterz-Najar and Rudel, 1967a), action at the ovarian level (France and Pincus, 1964, Yadava and Laumas, 1969), and rapid transport of the ovum from the fallopian tubes to uterus leading to failure of fertilization (Chang, 1967a, 1967b) have been made. It has become evident
that the drug, dosage and mode of administration would determine its site and mechanism of action.

Further progress in this area requires a major breakthrough. Diczfalusy (1971) in his lecture in the Nobel Symposium has reviewed and listed five factors which are interfering with further developments in the field of contraceptive steroids. These relate to a lack of knowledge on the distribution, transport and metabolism of the various contraceptive steroids in the human and animal species, especially those animal species which are used for toxicity studies. A knowledge of their action at the cellular level is lacking.

The objective of the work taken up in this thesis was to learn about the distribution, metabolism, excretion and site of action of progestational steroids.

The progestational steroids: one norethynodrel belonging to 17α-ethynyl 19-nor steroid category and the other chlormadinone acetate belonging to the 17α-acetoxy group were used to study their uptake in the reproductive tract, various parts of the brain, metabolic and excretory tissues of the rat, both by single injection
and constant infusion techniques. These studies were aimed to understand the patterns of distribution, disappearance and localization of the progestational steroids. The manner in which these progestational steroids modify the uptake of $^3$H-estradiol in the uterus has been investigated to learn about the mechanisms by which these progestational steroids act at the uterine level (Chapter I). The fate of these progestational steroids in the body has been followed. Their excretion in the milk of lactating women and goats has been investigated. The possibility of the excretion of estrogenic activity due to the progestational steroids has been explored (Chapter II). Besides milk, the progestational steroids are excreted through urine and faeces. The patterns of disappearance of the progestational steroid in the blood, its metabolic clearance rate and profiles of excretion in the urine have been studied (Chapter III). While the major part of the administered steroid is metabolized and excreted, a very small amount is taken up at the site of action to produce its effect. The effect of these small amounts on the corpus luteum function
either through hypothalamic-pituitary axis or a
direct action on the ovary has been investigated
by measuring plasma progesterone levels using a
highly sensitive radioimmunoassay (Chapter IV).
Cumulatively, these investigations have thrown
light on the fate of the progestational steroids
in the body, and provided guidelines for the mechanism
of action of these steroids.