

# **THE POSSIBLE APPROACH TO FERTILITY REGULATION**

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## **INTRODUCTION:**

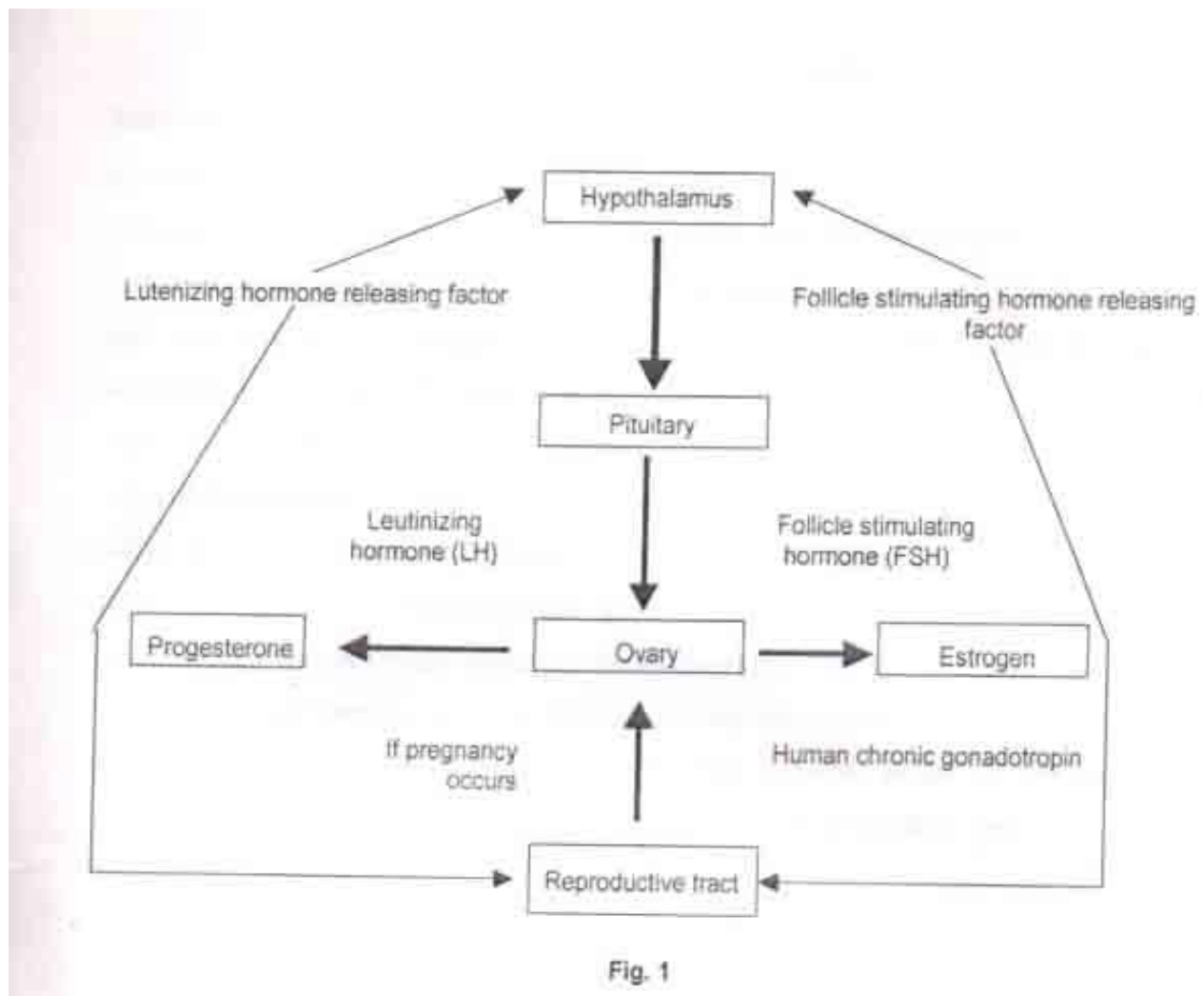
The population control is the most important socio-economic problem and it needs urgent attention. Of the many problems being faced by humanity one which can be termed as the root cause of many others is that of rapid population growth. It hampers the economy and general public health of a country and is ominous especially to the countries of third world. The outburst of human population is causing fast depletion of the enormous existing resources globally. If the trend continues, it shall lead to devastation much before time. Thus, efforts to check fertility may bring improvement in the quality of life.

## **MAIN BODY:**

Contraceptive devices are in use since the dawn of civilization but mainly among a handful of educated population. With the increase of mass education and awareness, people are realizing the importance of contraception for better livelihood, education and cosy family affairs.

The logical solution to the existing problem is to prevent unrestricted population growth. There is an urgent need, therefore, to generate mass motivation for voluntary fertility control. These efforts can, however, be critically handicapped unless simple and efficient contraceptive means are made available for the must use. Development of 'Ideal' contraceptive methods that are economical, convenient to use, emotionally and socially acceptable, fully reversible and without any collateral effects are thus the foremost challenge.

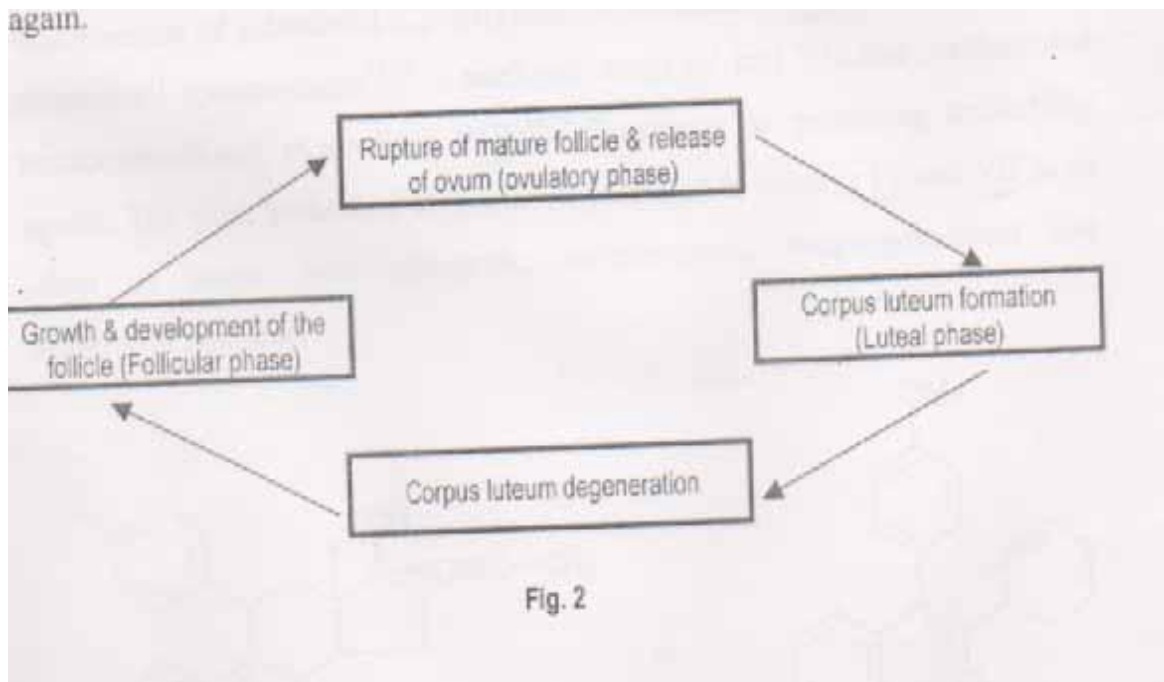
The female reproductive cycle is controlled through integrated system involving hypothalamus, pituitary gland, ovary and reproductive tract (Fig. I)



The hypothalamus exerts its action on the pituitary gland through follicle-stimulating hormone releasing factor (FSH-RF) and luteinizing hormone releasing factor (LH-RF) which initiate the release of glycoproteins FSH and LH from pituitary gland. A third protein luteotropic hormone (LTH), also known as prolactin, is involved in cyclic ovarian function.

The two main pituitary gland hormones, FSH & LH regulate the ovary and its production of sex hormones. FSH is responsible for the development of immature graafian follicle in the ovary and cannot induce ovulation alone but in conjunction with LH promotes follicle growth and increases secretion of estrogen. Due to negative feedback mechanism, the released estrogens inhibit the production of FSH and stimulate the output of LH and thus the level of LH is increased at midpoint in the menstrual cycle and bring about ovulation. Thus during menses the level of LH is extremely low while concentration of FSH reaches its high level.

Once the ovulation has taken place, LH induces luteinization of the ruptured follicle which leads to the formation of corpus luteum and increases the level of progesterone and suppresses the production of LH. Once the corpus luteum is formed, it begins to degenerate towards menses and thus the level of progesterone and estrogen decline. The major events are summarized in Fig.2. During reproductive cycle endometrium, a part of genital tract passes through different phases depending upon the secretion of the steroidal hormones from the ovary. The development of follicle approximately takes about 10 days is referred to as *follicular phase*. During this period proliferating of endometrium takes place owing to estrogenic stimulation. The luteal phase which brings about ovulation lasts for 14 days and ends at menses. In absence of pregnancy the levels of estrogen and progesterone decline resulting shedding of endometrium. Because of low level of estrogen and progesterone, hypothalamus begins the release of FSH-RH and cycle starts again.



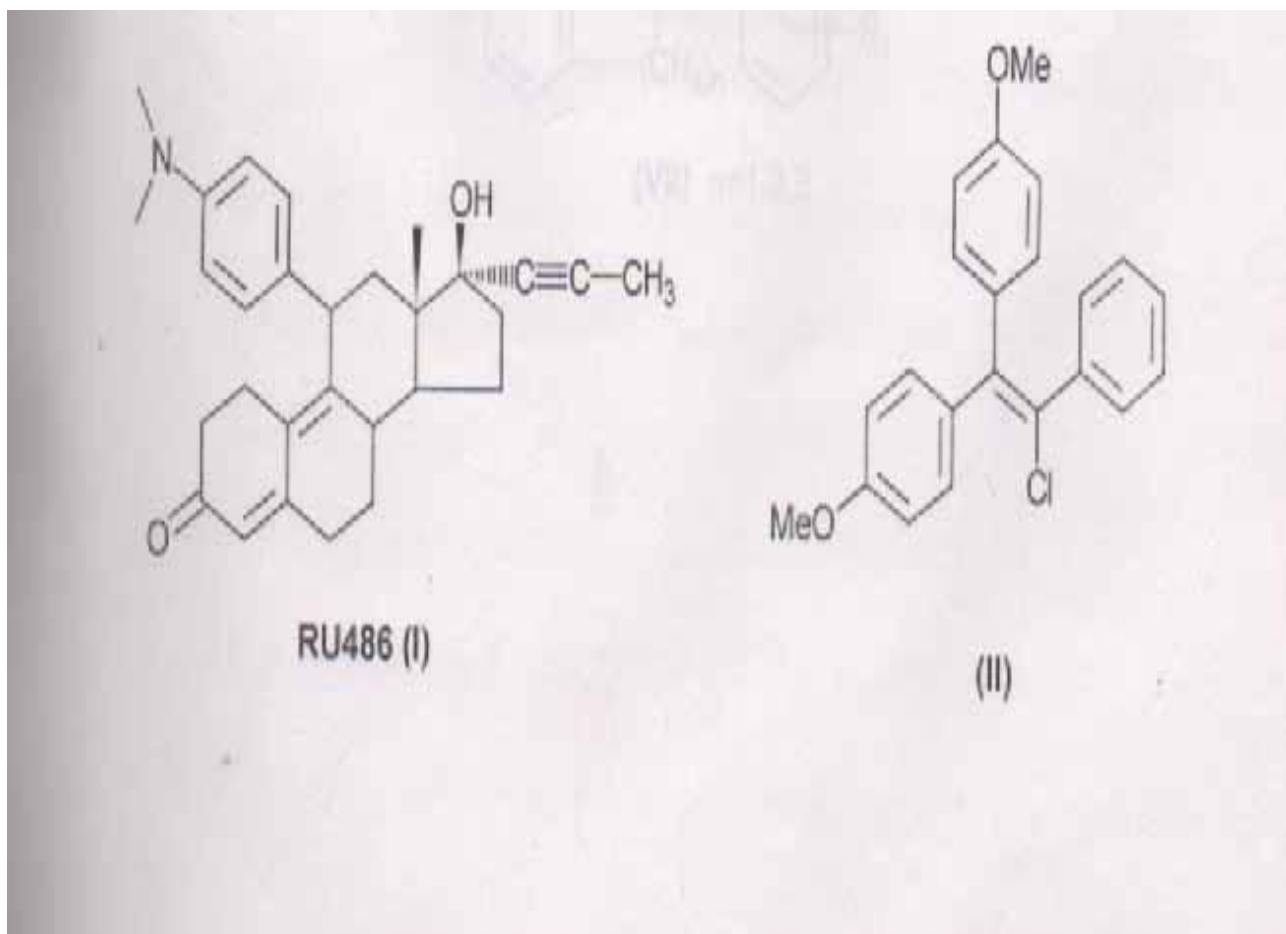
In case pregnancy occurs the menstrual cycle is interrupted by the release of a new gonadotropin produced by human placenta known as human chorionic gonadotropin (HCG) which increases the life span of the corpus luteum. Under this condition corpus luteum provides adequate level of estrogen and progesterone to maintain the pregnancy.

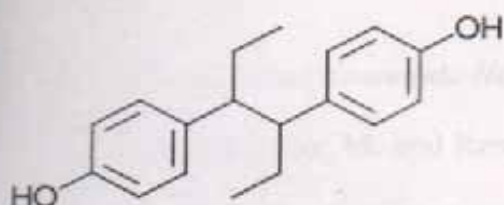
Thus, for the establishment and maintenance of successful pregnancy a proper balance of estrogen-progesterone, regulated by interplay of hypothalamic, pituitary and ovarian functions is of prime importance. An interference with this critical balance or any modification in the action of these hormones at the target sites

terminates the pregnancy and this has been an attractive basis for the designing and development of oral contraceptives. Similarly, development of progesterone antagonist appears to be a better and safer approach to fertility regulation. Unfortunately, the entire progesterone antagonist known till date have unfavourable side effects also. To date, the best antiprogesterin is RU486 (I)<sup>1-4</sup> but it has been declared as controversial drug due to its higher failure rates because it exhibits antiglucocorticoid activity also<sup>5,6</sup>. So work in this area may not be rewarding.

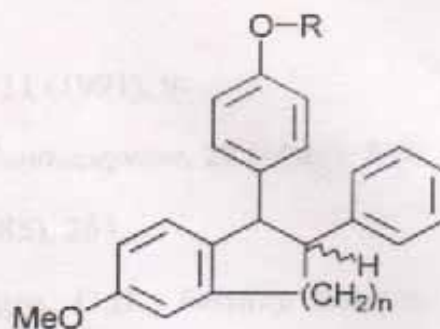
## CONCLUSION:

The emergence of oral antifertility activity in estrogenic/antiestrogenic triarylethylene(s)ethane(s) (II and III)<sup>7,8</sup> class of compounds led to the development of substituted 1,2-diarylbenzocycloalkanes (IV)<sup>9,10</sup>, corresponding chromans<sup>11</sup> (centchroman<sup>12,13</sup> –marketed drug) (V and VI) and 2-substituted benzocycloalka© pyrazolines (VII)<sup>14,15,16</sup> systems as promising antifertility agents.

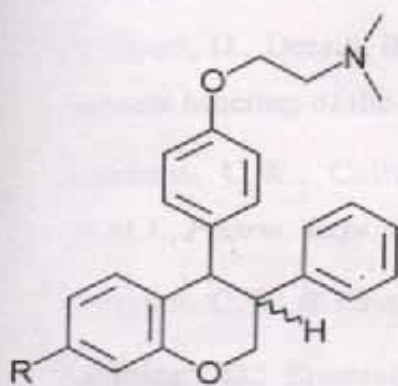
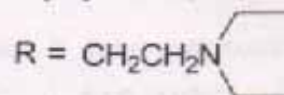




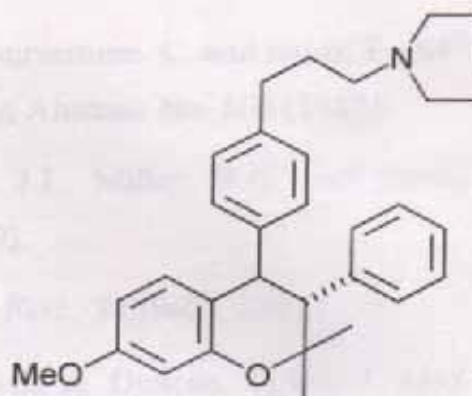
(III)



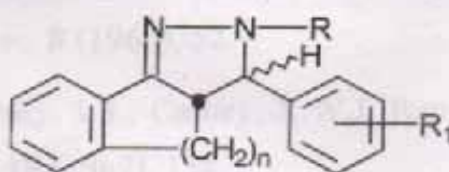
(IV)  $n = 1, 2$



(V)



(VI)



(VII)  $n = 1, 2, 3$

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