3.6 Gonadoliberin (LRF)

Gonadoliberin (LRF) was isolated from porcine and ovine hypothalamic extracts. Its highest concentration is found in the hypothalamus. However, it is also reportedly present in extrahypothalamic central nervous regions, blood, urine, and placenta. LRF acutely stimulates LH and FSH secretion. Single injections induce ovulation and increase steroid secretion. Additionally, there is evidence that it can act on the central nervous system to modulate sexual behaviour. Paradoxically, its long-term administration is associated with antigonadal effects, which include termination of pregnancy, decreased gonadal weights, and lowered steroid secretion. This is possibly due to desensitization at pituitary and gonadal levels and through alterations in steroidogenesis.

The sequence of isolated endogenous LRF was confirmed by synthesizing the decapeptide using solid-phase techniques. Once purified, the synthetic product showed the same physicochemical and biological properties as the natural porcine LRF.

Potent and long-acting analogues of LRF have been designed. These peptides generally have a D-amino acid at the 6-position. The LH-releasing potency of the most potent agonists (i.e. analogues which have similar biological effects) are about one hundred and fifty times that of LRF. Potent antagonists also have been