

## Effects of the combination of levonorgestrel and quinestrol on reproductive hormone levels and their receptor expression in female Mongolian gerbils (*Meriones unguiculatus*)

Ly, X.<sup>1</sup>, Guo, Y.<sup>2</sup>, Shi, D.<sup>1</sup>

<sup>1</sup>College of Agriculture and Biotechnology, China Agricultural University, Beijing 100193, China, shidazhao@cau.edu.cn

<sup>2</sup>National Agricultural Technology Extension and Service Center, Beijing 100125, China

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The effects of treatment with a combination of levonorgestrel and quinestrol (EP-1; ratio of 2:1) on reproductive hormone levels and their receptor expression in female Mongolian gerbils were examined. In the time-dependent experiment, fifteen gerbils were given a single intragastric dose of EP-1 (50 µg/g body weight) at dioestrus and killed 7, 14, or 21 days later (n=5 animals per group). Control animals (n=5) received peanut oil at dioestrus and were killed on Day 0. The ovaries and uteri were collected for RNA extraction. Blood samples were collected before euthanasia. In the second, dose-dependent experiment, another twenty gerbils (n=5 per treatment group) were given EP-1 intragastrically once at 0, 2, 10, or 50 µg/g body weight at dioestrus. The control group was given peanut oil. Blood samples were collected at 7 days after administration. The gerbils were killed 21 days after treatment. The ovaries and uteri were collected for RNA extraction.

The effects of EP-1 treatment were time- and dose-dependent. Serum follicle-stimulating hormone (FSH) and luteinizing hormone (LH) decreased, whereas serum estradiol (E2) and progesterone (P4) increased after EP-1 treatment compared to control treatment. EP-1 down-regulated the mRNA expression of the follicle-stimulating hormone receptor (FSHR) and the estrogen receptor (ER) β in the ovary. EP-1 up-regulated the mRNA expression of the luteinizing hormone receptor (LHR) and the progesterone receptor (PR) in the ovary as well as ERα and PR in the uterus of Mongolian gerbils. However, EP-1 had no obvious effects on ERα mRNA expression in the ovary.

The current study has demonstrated that the effect of EP-1 on the expression of ER subtypes is tissue-specific in Mongolian gerbils. EP-1 disrupted the reproductive endocrinology of the Mongolian gerbil. The findings suggest that the effects of EP-1 on reproductive hormone levels and their receptor expression in Mongolian gerbils may be a result of the synergistic actions of levonorgestrel and quinestrol with quinestrol playing the major role.

Keywords: EP-1, reproductive hormone, reproductive hormones receptors