



EP-1

Quinestrol (E) and Levonorgestrel (P)

Brand name: : AntiFert® Content by weight /volume 0.0025% levonorgestrel and 0.0025% quinestrol, granules for oral use

Main Active Ingredient: levonorgestrel and quinestrol

Indications for use: reduction of the fertility of rodents (in both litter size and pregnancy rate)

Registered: in Tanzania (Registration No. RO/012, Ministry of Agriculture, Tanzania)

Manufacturer: Sokoine University of Agriculture, Tanzania, and Institute of Zoology, Chinese Academy of Sciences.

Regulatory Status: rodenticides

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General Description

Quinestrol (E) and levonorgestrel (P) are two synthetic hormones used for birth control in humans since the 1960s. Quinestrol and levonorgestrel, referred to as EP-1, have long been explored to reduce fertility of rodents and require multiple doses to affect reproduction. For instance oral administration of quinestrol and levonorgestrel (10-200 ppm (parts per million); E:P = 1:2) for a few days could suppress reproduction of three wild rodent species (Brandt's vole *Lasiopodomys brandtii*, striped field mouse (*Apodemus agrarius*) and Mongolian gerbil *Meriones unguiculatus*) in laboratory and field trials (Zhao et al. 2007; Lv and Shi 2012; Chen et al. 2021).

Zhang et al. (2006) demonstrated that a single baiting event, with baits containing 10 ppm and 30 ppm of EP-1 (E:P = 1:2) significantly reduced reproduction of Greater long-tailed hamsters *Tscherskia triton* in laboratory tests. Liu et al (2012) demonstrated that a single baiting of 50 ppm EP-1 (E:P = 1:2) significantly reduced reproduction of Plateau pika *Ochotona curzoniae* in Qinghai-Tibetan plateau. EP-1 has been widely tested in many species in the world (see review by Jacoblinnert et al. 2022). On August 22, 2020, EP-1 was registered as AntiFert® in Tanzania under the cooperation between the Sokoine University of Agriculture, Tanzania and the Institute of Zoology, Chinese Academy of Sciences.

Dosage and Administration

The doses of EP-1 causing anti-fertility effects on rodents often range from 1 to 10 mg/kg body weight or 10–50 ppm if delivered directly in the mouth (in laboratory trials) or in baits (Zhang et al. 2004; Zhao et al. 2007; Liu et al. 2012; Massawe et al. 2018; Selemani et al. 2022; Stuart et al. 2022; Chen et al. 2022). One week is sufficient for EP-1 in baits to have an antifertility effect on rodents in the laboratory, and a single baiting is likely to suppress reproduction of rodents for 3-4 months in field conditions (3 kg/ha, 0.005% EP-1; Liu et al. 2012). Females often show enlargement (edema) of the

uterus in response to E and EP-1. Males often show reduction of weight of testis, epididymis, and seminal vesicle in response to E and EP-1 (Liu et al. 2012).

AntiFert® baits are recommended to be delivered before or during the breeding season. Pellet piles are placed where rodents are active, such as rodent pathway or near active burrow entrance, or in the active burrows. A pellet pile generally contains 5-20 g baits. To reduce non-target uptake of baits and protect them from sunlight and rain, the bait is best placed in bait stations made of short lengths of plastic pipe or bamboo (Imakando et al. 2022).

Approximately 3 kg/ha pellets have been delivered in various studies, but the amount of bait should be adjusted based on the rodent density. A single bait delivery is often able to control a population in seasonal breeding animals. Twice baiting is necessary for rodents breeding throughout the whole year.

Toxicity and Side Effects

Based on the data available in the literature quinestrol is moderately toxic and levonorgestrel is unlikely to present acute toxicity. Both quinestrol and levonorgestrel affect reproduction of people and non-target animals, often temporarily. In terms of toxicity, the LD50, i.e. the amount ingested that kills 50 percent of the animals, is 960 mg/kg in rats and 950 mg/kg in mice (referred to ethinylestradiol administered orally) for quinestrol, and >108 mg/kg in *Coturnix coturnix* (oral). The LD 50 of Levonorgestrel (oral) is 5010 mg/kg in rats and mice.

Quinestrol and levonorgestrel are easily and quickly decomposed by microorganisms in the natural environment (soil or water). Their half-life is about 2 weeks in soil and 2-6 hours in water (Tang et al. 2012 a and b). In a laboratory condition, EP-1 delivered in the mouth could delay production of eggs by domestic chickens (He et al. 2021). EP-1 oral baiting showed little effect on bird abundance and diversity in a field

test, except on the abundance of white-rumped snowfinch (*Montofringilla taczanowskii*) which was reduced (Qu et al. 2015).

Because the dosage used is relatively low in field conditions (3 kg pellets per ha), and quinestrol and levonorgestrel can be

decomposed by microorganism quickly, it is very hard to detect the residue of quinestrol and levonorgestrel in soil and water after the baits are used. The antifertility effect is usually reversible within 3-4 months.

References

- Chen X, Hou X, Feng T, Han N, Wang J, Chang G (2022). *Anti-fertility effect of levonorgestrel and/or quinestrol on striped field mouse (Apodemus agrarius): Evidence from both laboratory and field experiments*. - Integrative Zoology 17, 1041–52.
- He S, Zhou X, Wang Y, Zhang M, Wu K (2021). *Assessment of non-target toxicity effects of synthetic estradiol, quinestrol, in chickens*. - Integrative Zoology 17, 1053–1062.
- Imakando CI, Fernandez-Grandon GM, Singleton GR, Belmain SR (2022). *Impact of fertility versus mortality control on the demographics of Mastomys natalensis in maize fields*. - Integrative Zoology 17, 1028-1040.
- Jacobinnert K, Jacob J, Zhang Z, Hinds LA (2022). *The status of fertility control for rodents—recent achievements and future directions*. - Integrative Zoology, 17, 964-980.
- Liu M, Qu J, Yang M, Wang Z, Wang Y, Zhang Y, Zhang Z (2012). *Effects of quinestrol and levonorgestrel on populations of plateau pikas, Ochotona curzoniae, in the Qinghai–Tibetan Plateau*. - Pest Management Science 68, 592–601.
- Lv X, Shi D (2012). *Combined effects of levonorgestrel and quinestrol on reproductive hormone levels and receptor expression in females of the Mongolian gerbil (Meriones unguiculatus)*. - Zoological Science 29, 37-42.
- Massawe AW, Makundi RH, Zhang Z, Mhamphi G, Liu M, Li HJ, Belmain SR (2018). *Effect of synthetic hormones on reproduction in Mastomys natalensis*. - Journal of Pest Science 91,157-68.
- Qu J, Liu M, Yang M, Zhang Z, Zhang Y (2015). *Effects of fertility control in plateau pikas (Ochotona curzoniae) on abundance and diversity of native birds on Tibetan Plateau*. - Acta Theriologica Sinica 35, 165–9.
- Selemani M, Makundi RH, Massawe AW, Mhamphi G, Mulungu LS, Belmain SR (2022). *Impact of contraceptive hormones on the reproductive potential of male and female commensal black rats (Rattus rattus)*. - Integrative Zoology 17, 991-1001.
- Stuart AM, Herawati NA, Risnelli J, Sudarma I, Liu M, Zhang Z, Li H, Singleton GR, Hinds LA (2022). *Reproductive responses of rice field rats (Rattus argentiventer) following treatment with the contraceptive hormones, quinestrol and levonorgestrel*. - Integrative Zoology 17, 1017–1027.
- Tang T, Qian K, Shi T, Wang F, Li P, Li J, Cao Y (2012a). *Photodegradation of quinestrol in waters and the transformation products by UV irradiation*. - Chemosphere 89, 1419–25.
- Tang T, Shi T, Li D, Xia J, Hu Q, Cao Y (2012b). *Adsorption properties and degradation dynamics of endocrine-disrupting chemical levonorgestrel in soils*. - Journal of Agriculture and Food Chemistry 60, 3999–4004.
- Zhang Z, Meirong ZH, Xiaoping CA, Yanling WA, Fusheng WA, Jianxu ZH (2006). *Effects of a contraceptive compound (EP-1) on reproductive organs of male greater long-tailed hamsters (Tscherskia triton)*. - Acta Theriologica Sinica 26: 300.
- Zhao M, Liu M, Li D, Wan X, Hinds LA, Wang Y, Zhang Z. (2007). *Anti-fertility effect of levonorgestrel and quinestrol in Brandt's voles (Lasiopodomys brandtii)*. - Integrative Zoology 02, 260-268.



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