

Abstract:

A series of studies was carried out to investigate feasibility of chemical fertility control in wild rabbit populations. Initial trials were designed to investigate *in vivo* kinetics and bioavailability properties of MPA in rabbit plasma and effects of a single oral dose on fertility in females. MPA was incorporated into carrots or feed pellets before administration. Plasma concentration of MPA reached maximum levels 1 - 12 h post treatment and declined to undetectable values after 1 or 8 days depending on dosage. An oral dose of 10 mg MPA/rabbit caused complete infertility in females mated 1 day but did not affect fertility in those mated 8 days after treatment. Animals orally dosed with 100 or 1000 mg MPA were infertile when mated 1 day but not 29 days post treatment. It was concluded that MPA is absorbed in the gastrointestinal tract following incorporation in feed of rabbits, its bioavailability is dose-dependent in the dose range tested and a single oral dose of 10 mg or more causes complete infertility for at least 1 day following treatment. Further trials were conducted to investigate the mode of action of MPA in female rabbits. In one such experiment, rabbits were mated following a single oral dose of MPA and post mating plasma progesterone and LH concentration measured in order to determine ovarian and pituitary endocrine activity. There was no post mating increase in plasma hormone concentrations until 4 days following MPA treatment. A single oral dose of 10 mg MPA provided a contraceptive effect in female rabbits for a period of 4 days and this appeared to be directly related to its bioavailability. In another experiment, rabbits mated 3 - 6 days following MPA treatment were killed 28 - 30 h post mating. The ovaries were examined for ovulation sites, oviducts flushed with saline solution and the washings examined for embryos. MPA either blocked ovulation or lowered the ovulation rates of rabbits mated 3 days post treatment. Rabbits mated 4 - 6 days had normal ovulation rates. There were no effects of MPA on oocyte fertilization. In an experiment to determine if MPA acts at the level of the hypothalamus or the pituitary, ovariectomised rabbits were injected *i.m.* with 250 ng GnRH before and after a single oral dose of MPA. Although MPA significantly lowered basal plasma LH concentration, response of LH secretion to the GnRH challenge was not suppressed by its administration. These results indicate that a single oral dose of MPA affects the ovulatory process in mated rabbits for up to 4 days by blocking the preovulatory LH surge and ovarian endocrine activity, and that the effect is directed mainly at the level of the hypothalamus. In another series of experiments, MPA was administered to mated rabbits in early-, mid or late-pregnancy and effects on conception, pregnancy and parturition determined. MPA had no effects on conception or pregnancy. However, when administered as a single large oral dose (1000 mg/rabbit) or as low multiple doses (10 mg/rabbit/day x 5) in late-pregnancy, MPA significantly inhibited normal parturition. Nonetheless, the mechanisms of the effects of MPA on parturition could not be determined and there is a need for further study on this potentially very important effect of MPA.