Evaluation of Non-hormonal Contraceptive Rings in Rabbits

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Introduction: At present, female sterilization, oral contraceptives, and condoms are the three most widely used methods of contraception in the developed world.[1] With the exception of barrier methods, such as male or female condoms and spermicides (used in combination with condoms) and permanent contraceptive methods, such as sterilization and vasectomy, existing birth control methods rely on hormones to suppress ovulation. One of the latest commercial products is Nuva Ring™, a hormonal intravaginal ring made of ethylene-vinyl acetate copolymer.[2] However, health risks are a growing concern among women taking hormone-based contraceptives, which may increase the incidence of cervical and breast cancer.[3] This led to the exploration of new, non-hormonal, controlled release intravaginal contraceptives.[4] The objective of the present study is to test the contraceptive efficacy of one such device using a rabbit model. This is similar to those reported in the literature but adapted for this particular contraceptive device.[5,6] The non-hormonal contraceptive intravaginal device of the present study consists of a silicone-based ring reinforced with an absorbable yarn[7] affixed to a knitted mesh. The reinforcing yarn and mesh are made of the same material. The silicone portion of the ring contains ferrous gluconate (FeG), which causes complete spermatostasis, and ascorbic acid (AA) to increase the viscosity of the cervical mucus. FeG release from a fiber reinforced silicone ring was reported[8] to continue over 30 days making these rings viable candidates for intravaginal contraception.

Materials and Methods: The knitted mesh portion of the ring is constructed from an absorbable multifilament yarn made of a segmented lactide copolymer.[9] The mesh is attached to a scaffold support made from the same multifilament yarn used to make the mesh. To prepare the ring, a two-part biomedical-grade silicone was mixed with ferrous gluconate, ascorbic acid, and other additives to control the pH of the ring placement site in the vagina. This mixture was then injected into a mold that was preloaded with the reinforcing yarn/mesh mentioned above and placed into an 80ºC oven until proper curing had been achieved. The mold cavity was constructed to produce a ring with an outside diameter of 20 mm and an inside diameter of 13.6 mm. A diagram with the ring dimensions used in the rabbit study is shown in Figure 1. These dimensions are based on rabbit cadaver vaginal tract measurements. The animal study consisted of 8 virgin female New Zealand White rabbits and 3 breeder males. Of the 8 females, 3 contained no device (control) and 5 contained devices with ferrous gluconate and the noted additives. Rabbits were mated with the breeder males 3-4 days after placement of the rings in the vagina. Pregnancy was confirmed when the rabbits were euthanized 14 days after breeding. Following euthanasia, vaginal tissues were collected from 6 rabbits (1 control and 5 containing the devices) and placed in 10% formalin for microscopic evaluation. It should be noted that the rings used for this study are a miniaturized version of the contraceptive device proposed for human use.

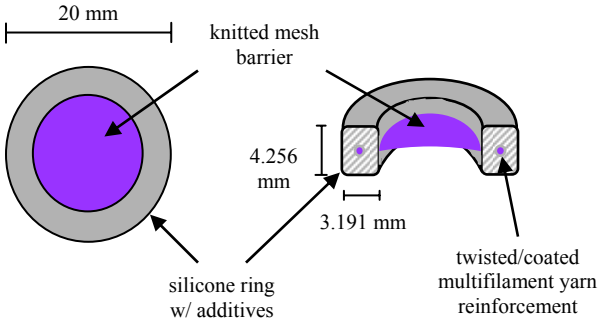

Figure 1. Miniaturized 20 mm design of the ring intended for human use.

Results and Discussion: Table I summarizes the animal study and breeding results. Pregnancy was prevented in all five female rabbits that received the 20 mm rings with the knitted mesh and ferrous gluconate. The control rabbit and five does treated with the ringed mesh displayed minimal leukocytic infiltrates within the submucosa or the lumen of the vagina.

Table I. Breeding Results from Rabbit Study

Type of Ring	Total Females Bred	Pregnant	Not Pregnant
Controls (no ring)	3	3	0
Ring w/ knitted mesh and FeG	5	0	5

Conclusions: Results show that the non-hormonal contraceptive ring examined in this study is effective in preventing pregnancy in rabbits, and could lead to further advancements in non-hormonal contraception for human use.

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