Abstract

NON-HORMONAL INTRA-VAGINAL CONTRACEPTIVES FROM A BIODEGRADABLE HYDROGEL DELIVERY SYSTEM (BIORING)

Weill Medical College of Cornell University
Dept. of OB/GYN
1300 York Avenue
New York, NY 10021
USA

Recent studies have shown an increase in the incidence of cervical and breast cancer among women who use hormonal contraceptives for more than five years. There is a need for a non-hormonal contraceptive, which is safe, effective, would by passes the systemic effect, allow women the coital independence and protect against pelvic infections and other sexually transmitted diseases (STDs).

A variety of hormonal and non-hormonal contraceptive methods are available to women today. However, sexually active women still continue to risk unwanted pregnancies and sexually transmitted diseases. We
describe here the development of a novel non-hormonal, biocompatible programmed release intravaginal drug delivery device (BioRing) using a biodegradable hydrogel matrix. The BioRing is composed of a core surrounded by four concentric sheaths composed of dextran, copolymers of polylactide and ε-caprolactone for time release of desired dose. The hydrogel based BioRing was incorporated with ferrous gluconate as a spermicidal agent, L-ascorbic acid as a reducing agent to increase the viscosity of cervical mucus and mixtures of polyamino-polycarboxylic acid (Ampholines) as the pH modulator to sustain normal vaginal pH (between 4-5). Daily eluates from the hydrogel were analyzed for pH levels and spermicidal activity. In vitro as well as in vivo studies in estrus female rabbits, effect on the cervical mucus and effect on vaginal flora as well as the sterility of the BioRing was evaluated. Eluates, in vitro, up to sixteen days caused complete spermeostasis within 30 seconds, increased the viscosity of the cervical mucus similar to that found in luteal phase of women's menstrual cycle, and sustained the vaginal pH between 4.0 and 5.0. The combined effect of the agents was demonstrated by sperm penetration tests. The eluates did not affect the normal vaginal flora. In vivo studies, the anterior vagina of three estrus female rabbits were instilled with the hydrogel matrix, and after 4 hours the rabbits were inseminated with the semen of a fertile male rabbit. Post-insemination flushes from the vagina of female rabbits were tested for sperm mortality showed that all the sperm were immobile. Addition of
human tubule fluid failed to reanimate the sperms. External genitalia of female rabbit appeared to have no inflammatory reaction. The entire ring was examined for 28 days and no bacterial growth was noted.

The biodegradable hydrogel is being currently developed as an intravaginal ring, for phase I study in humans. The ring is 5.33 cm in diameter and 0.54 cm wide. The flexibility (MTS) maximum load for 1 inch deflection is 1.70N-2.31N to make it easy to insert and remove. Such a device can also be used to deliver anti-HIV as well as other drugs to protect from pelvic infections.