

# Biostable Non-hormonal Contraceptive Antifungal Intravaginal Ringed-mesh: A Preliminary Study

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**Statement of Purpose:** For over ten years, Poly-Med has continually explored the development of proprietary bioactive intravaginal ring systems. These efforts included (1) studies on composite absorbable biodegradable rings for controlled drug delivery; (2) studies on partially absorbable fiber-reinforced composite rings for controlled drug delivery; (3) development of a contraceptive intravaginal ringed-mesh; and (4) studies on the development of multicomponent bioactive intravaginal rings.<sup>1-4</sup> Proprietary intravaginal ring systems were highlighted in previous technical reports on (1) the spermistatic effect of a non-hormonal contraceptive ring; (2) antibacterial non-hormonal contraceptive ring; and (3) antifungal ring.<sup>5-8</sup> This provided strong incentive to pursue the current study on a novel ringed-mesh with a bioactive agent that exhibits not only antifungal, but also spermistatic activity.

## Materials and Methods:

Intravaginal rings were prepared by melt blending an ethylene vinyl acetate (EVA) copolymer, polyethylene glycol (~35 kDa), and miconazole nitrate. The blended material was then injected into ring molds preloaded with a woven polypropylene monofilament mesh (~75 micron pore size). Intravaginal rings had an outer diameter of 55 mm and inner diameter of 40 mm.

To measure miconazole release, each ring was incubated in 50 mL PBS (pH 4.5) at 37°C for 24 hours, after which eluents were collected and replenished daily for 28 days. Portions of collected eluents were reserved for HPLC and microbiological analysis.

The effect of eluents on the growth of *C. albicans*, commonly known as yeast, and *L. vaginalis*, a beneficial bacteria found in the normal vaginal flora, was tested. Briefly, 100 µL of each eluent was added to 4.9 mLs of broth inoculated with either organism.<sup>7,8</sup> Controls were untreated inoculated broth. Samples containing *C. albicans* were incubated at room temperature, while samples containing *L. vaginalis* were incubated at 37°C in the presence of 5% CO<sub>2</sub>. After approximately 24 hours, relative absorbance was measured using a spectrophotometer (600 nm wavelength). Sample absorbance values were normalized by that of the control to yield percentages. Inhibition was reported as the percent decrease compared to controls.

The spermistatic activity of miconazole in aqueous solutions was also evaluated as described earlier.<sup>6</sup> Briefly, a miconazole solution in saline was added to a pooled sperm sample. After a specified time period (10 minutes or 12 hours), sperm motility was recorded.

**Results:** The results in Table I show that miconazole was released for at least 28 days. In addition, inhibition of *C. albicans* was observed with little or no effect on the beneficial *L. vaginalis* (Figure 1). Preliminary data also

shows that sperm motility is decreased by miconazole at the concentration tested (Table II).

**Table I. Miconazole Release from Intravaginal Ring**

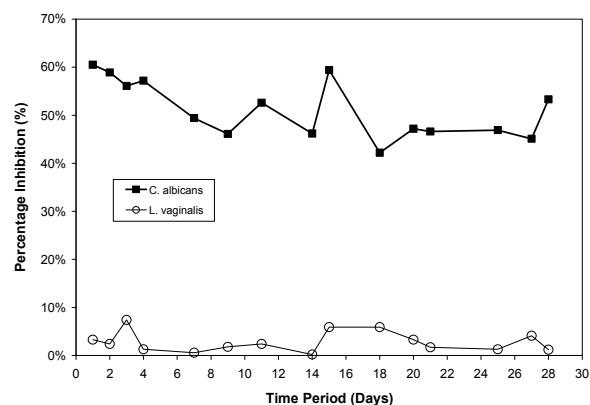
Time (Days)	Incremental Drug Release (micrograms/ml)	Cumulative Drug Release (mg)
1	7.80	0.390
7	2.86	0.981
14	3.88	1.476
21	3.92	2.352
28	3.97	3.128

**Table II. Effect of Miconazole on Sperm Motility**

Sample	Concentration (micrograms/ml)	Motility* after 10 minutes	Motility** after 12 hours
Saline Control	N/A (No drug added)	70%	Yes
Miconazole	55	44%	No

\*Reported as the percentage of motile sperm out of total number of sperm

\*\*Yes indicates there were motile sperm observed. No indicates there were no visible sperm observed.



**Figure 1. Inhibition of *C. albicans* and *L. vaginalis***

**Conclusions:** *In vitro* results of a non-absorbable, polymeric intravaginal ringed-mesh containing miconazole can potentially be used as a contraceptive intravaginal ring with antifungal properties.

## References:

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