An Antifungal Intravaginal Ring

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Statement of Purpose: Yeast infection is among the most common and serious forms of vaginal infections. Commonly prescribed treatments of vaginal yeast infection include the use of an orally administered large dose of fluconazole and vaginal cream containing miconazole. Systemic toxicity which may be associated with the use of fluconazole and the limited residence time and drug bioavailability (1 to 3 days) of the miconazole vaginal cream in the vagina evoked the need for a new controlled release intravaginal antifungal device capable of providing inhibitory doses for at least one week. This and Poly-Med's continued interest in intravaginal drug delivery systems containing non-hormonal contraceptive and antibacterial agents prompted the pursuit of a program on the development of an antifungal intravaginal ring (IVR) system denoted Mycoprene®.[1-8] The initial phase of the program deals with a 2-phase, non-absorbable polymeric IVR containing miconazole nitrate and available results of its antifungal properties are discussed in this communication.

Methods: To prepare the rings an ethylene vinyl acetate (EVA) copolymer, polyethylene glycol (PEG) with a M_w of ~35 kDa and miconazole were melt blended and pelletized. The pelletized material was then used to injection mold rings with the following dimensions: outer diameter of 55 mm and inner diameter of 40 mm. To study the inhibition of *C. albican* (target microbe) by the ring devices produced above, one quarter of each ring to be tested was cut from each ring and incubated in YM Broth that had been inoculated with *C. albicans*, a micro-organism commonly recognized to be responsible for yeast infection.[9] Testing was conducted at 30ºC. After incubation (18-22 hrs), optical densities were read on the spectrophotometer at a wavelength of 600 nm. Percent inhibition of each ring was determined by comparing the optical density of ring broth to the control tube's optical density. This method was also used to study the inhibition of *L.vaginalis* (non-target microbe).

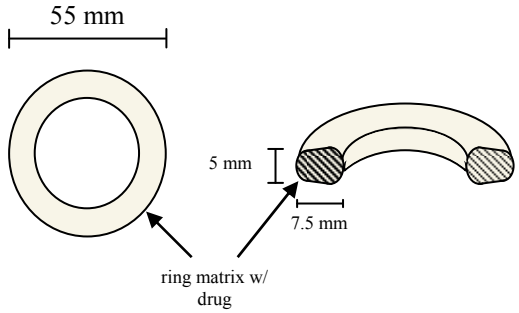

Figure 1. Mycoprene I® Intravaginal Ring

Results: Figure 2 depicts the *in vitro* test results. Inhibition peaks at 80% after 1.6 days of release with an average inhibition of 45% over the course of ~14 days. As suspected, minimal or no effect is seen on *L. vaginalis*, the principal micro-organism of the useful vaginal microflora, over the course of this testing. A brief *in vitro* comparative study of Mycoprene I with a commercially available miconazole-containing topical cream formulation revealed the superiority of the Mycoprene I ring in terms of effective dose and duration of the inhibitory effect.

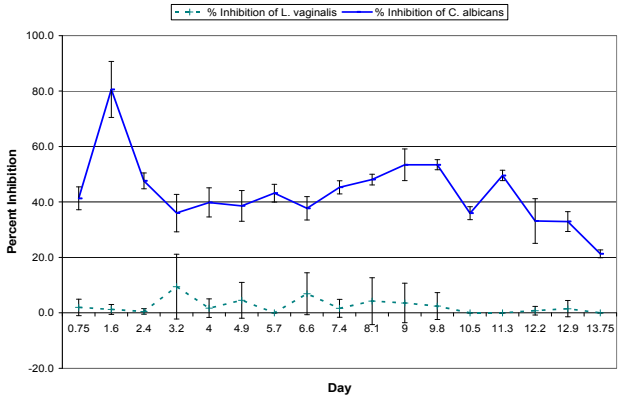

Figure 2. Average percent inhibition of *C. albicans* and *L. vaginalis* by IVR containing about 4% miconazole (Mycoprene I®).

Conclusions: *In vitro* results of a typical 2-phase, non-absorbable, polymeric intravaginal ring containing 2 to 6 percent of miconazole nitrate exhibits a significant inhibitory effect on *C. albicans* for about two weeks with practically no detrimental effect on *L. vaginalis*.

References:

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