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| **Novel multipurpose vaginal ring for non-hormonal contraception and sti/hiv prevention.** |
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| **Background:** According to the United Nations Sexual and Reproductive Health Agency (UNFPA), nearly half of all pregnancies (~121 million each year worldwide) are unintended. Despite increased choice and availability of contraceptive products, current contraceptive options are not meeting the needs of many women, as evidenced by high rates of typical-use failure and method non-use, switching, and discontinuation. Due to concerns about side-effects, contraindications, or increased health risks correlated with using synthetic estrogens, many women are opting for or would like to use a non-hormonal contraceptive method. Data also show that women prefer and are more likely to use a multipurpose prevention technology (MPT) product that simultaneously prevents pregnancy and sexually transmitted infections (STIs), including HIV. Here, we report a novel MPT vaginal ring concept incorporating three active ingredients – copper sulfate anhydrous (CSA), zinc sulfate monohydrate (ZSM), and DL-lactide (L, a cyclic dimer of lactic acid). Combined in a ring (CSA-ZSM-L), these three actives potentially offer broad spectrum spermicidal, antibacterial and antiviral activity against chlamydia, gonorrhea, bacterial vaginosis, HSV-2 and HIV while seeking to maintain an acidic vaginal fluid pH. |
| **Methods:** *In vitro* studies were conducted to evaluate the ability of CSA and ZSM to inhibit the motiity of human sperm. Matrix-type rings containing single actives (CSA, ZSM or L) and a combination of all three actives (CSA-ZSM-L) were manufactured from medical grade silicone elastomer (LSR 4350) by reaction injection molding at 115°C. Studies were conducted to assess lactide hydrolysis. Active substance and ring formulations were characterised by DSC and TGA. Rings were tested for *in vitro* release (IVRT) of lactide, copper ions and zinc ions by HPLC and ICP-OES. Mechanical testing (shore M hardness test and 5–20 mm compression test) was performed for all ring formulations. The ability of lactide to maintain an acidic vaginal pH via hydrolysis was evaluated *in vitro*. |
| **Results:** EC90 values for 50% reduction in the motility of human sperm were 11 and 65 mM for CSA and ZSM, respectively. CSA, ZSM and DL-lactide (L) – singly and in various combinations – were successfully incorporated into the vaginal rings. The weight, outer diameter and cross-sectional diameter of the lead candidate CSA-ZSM-L LSR4350 silicone elastomer rings (10% w/w each active) were 8.9 g, 57.0 mm and 7.3 mm, respectively. Copper ions, zinc ions and lactide/lactic acid were successfully released from the rings into deionized water: zinc ions – 5 mg/day and 150 mg for 30-day cumulative release, copper ions – 4 mg/day and 140 mg for 30-day cumulative release and lactic acid – 9–22 mg/day and 150 mg for 30-day cumulative release. pH in IVRT was maintained at the range 1.7–2.6. For the triple combination ring (CSA-ZSM-L), values for 20-mm compression force and shore M hardness were significantly different before and after 30-day IVRT and after 20-day drying at 40 ˚C (3.36 N, 1.69 N and 2.22 N; 65.8, 42.3 and 53.5, respectively), due the absorption of aqueous medium release medium. |
| **Conclusions:** The data support the further development of a CZL MPT vaginal ring formulation offering sustained release of zinc ions, copper ions and lactic acid. However, issues around ring swelling due to absorption of aqueous media by the hydrophilic actives will need to be resolved. |