Effects of Ascorbic Acid on Available Ferrous Iron from the Non-Hormonal Contraceptive Ovaprene® Ring

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Background: Currently, the most common forms of birth control are hormone-based contraceptives followed by sterilization and barrier methods.[1] With hormonal birth control, health risks due to side effects have become a primary concern. In hormonal contraceptives with progestin or estrogen, severe side effects (such as blood clots and cervical cancer) can occur. This has driven researchers to discover new methods of non-hormonal based contraception devices.[2,3,4] Spermatozoa are highly vulnerable to peroxidative damage through metal catalyzed lipid peroxidation.[5] In addition, ferrous iron has been identified as one of the more effective transition metals capable of lipid peroxidation. However, ferrous iron is rapidly oxidized at a pH dependent rate in aqueous solutions. In order to maintain iron in the ferrous state, the introduction of an antioxidant, ascorbic acid (AA), can be added to the system to control available ferrous iron. However, a low ascorbic acid to ferrous iron ratio must be achieved to prevent a suppression of lipid peroxidation by ascorbate. When the AA/ferrous sulfate ratios are greater than 7.75 an inhibitory effect of lipid peroxidation occurs.[6] The present study assesses the effect of the addition of ascorbic acid to the Ovaprene® (Poly-Med, Inc, Anderson, SC) ring in order to preserve the ferrous iron levels after released.

Methods: The rings used in this study were synthesized by physically mixing a two-part biomedical-grade silicone with ferrous gluconate (FG), AA, glycine, and polyglycolide microparticles. The mixture was injected into a cavity mold where a preloaded reinforced mesh resided. The mold was then heated to 80ºC until the two-part silicone cured. The mold cavities were shaped in a ring with an outside diameter of 55 mm and an inside diameter of 40.0 mm. Additional Ovaprene® rings were synthesized without ascorbic acid (OV-AA). A total of 13 rings were prepared for each ring type. Each ring type was submerged in 50 ml of simulated vaginal fluid and incubated at 37 °C for time periods of 1, 7, 14, 28, and 35 days. At each time point, the sample eluents were collected and assayed through spectrophotometric analysis under previously described methods.[7-8]

Results: A low molar ratio of ascorbic acid to ferrous gluconate must be achieved to impart reduction of iron to the ferrous state without the additional effect of inhibition of lipid peroxidation. As shown in Table I, the molar ratio of AA/FG is low enough at each time point to prevent inhibition of lipid peroxidation as was previously noted.[6]

Table I: Ratio of Ascorbic Acid/Ferrous Gluconate from the Ovaprene® Ring

Ratio of AA/FG					
1 day	7 days	14 days	21 days	28 days	31 days
5.81	0.91	0.98	0.65	0.53	0.50

The overall percent release of FG for the Ovaprene ® and OV-AA rings is outlined in Figure 1. As each component of the ring is insoluble in the silicone and soluble (in some form) in water, the absence of any component will affect the overall percent release of FG by creating a less porous silicone matrix.

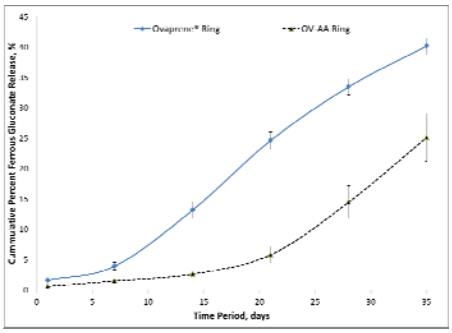

Figure 1: Overall 35 day Percent Release of Ferrous Gluconate

In Figure 2, the percentage of ferrous iron (of total iron) remains above 80% for the first 28 days in the Ovaprene® ring and has a minimum ferrous gluconate concentration of 180 µg/ml through 35 days. For rings without ascorbic acid, there is a significant reduction in percentage of available ferrous iron.

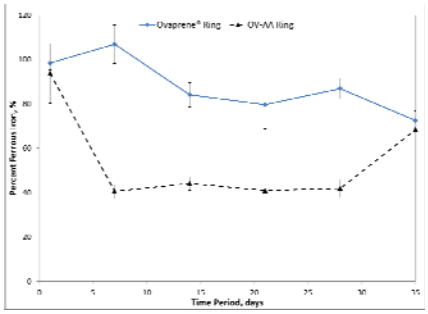

Figure 2: Percentage of Available Ferrous Iron from the Ovaprene® Ring

Conclusions: The results indicate that an effective amount of ascorbic acid is released from the Ovaprene® ring. At the concentration of ascorbic acid released, the Ovaprene® ring should be able to maintain a ferrous iron concentration that allows for efficacy without any inhibition of lipid peroxidation.

References:

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