



## Case Study: Dapivirine Vaginal Ring

### Assessing Uterine Contractility in Human Fresh Tissue

International Partnership for Microbicides (IPM) is a nonprofit organization dedicated to providing women with HIV-prevention strategies they can use to protect their own health, and to make them accessible where they are urgently needed.

*“The uterine contractility model represents a valuable tool for the safety evaluation of microbicides and other vaginal healthcare products”*

— Jeremy Nuttall, IPM

#### Executive Summary

The monthly dapivirine ring was developed by IPM to offer women a discreet option for HIV prevention. In 2020, the ring received a positive opinion from the European Medicines Agency for use by cisgender women ages 18 and over in developing countries. In its review, the EMA assessed evidence from hundreds of preclinical and clinical studies of dapivirine, including studies in human fresh tissue conducted by REPROCELL (Biopta).



## How We Helped

IPM researchers approached REPROCELL (Biopta) looking for a laboratory with the capability to perform a uterine contractility study. Following an initial consultation appointment with our predictive drug discovery team, they agreed to an *ex vivo* human tissue study. As fresh uterine muscle spontaneously contracts and relaxes *ex vivo*, our scientists were able to test dapivirine's potential effect on uterine contractility using an organ bath study.

## Methodology and Results

REPROCELL (Biopta) ethically-obtained fresh uterine muscle strips from five human tissue donors, and suspended them in organ baths. The positive control drug (oxytocin) caused an increase in the frequency of spontaneous muscle contraction (Fig 1). In contrast, dapivirine had no effect on uterine contractility, as did the negative control (forskolin, Fig 1).

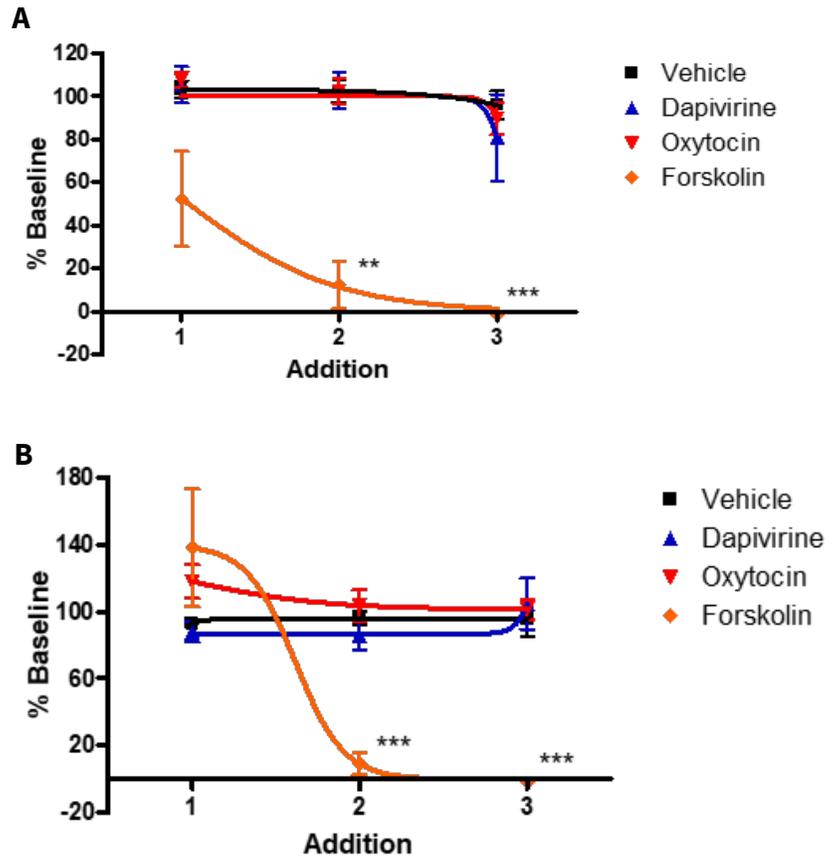
## Future Plans

In 2020, the DPV-VR received a positive opinion from the EMA, making it the first microbicide to do so.

The EMA assessed evidence from hundreds of preclinical and clinical studies of dapivirine, including studies in human fresh tissue conducted by REPROCELL (Biopta).

IPM is now developing a dapivirine ring that can be used for three months at a time.

**For more information about outsourcing fresh human tissue studies, visit [reprocell.com](http://reprocell.com)**



**Figure 1:** Graphs showing the effect of cumulative concentrations of vehicle, dapivirine, oxytocin and forskolin on spontaneous contraction in human uterine muscle strips. The addition of oxytocin had no effect on the peak area, however oxytocin caused an increase in the frequency of contractions (A)\*\* =  $p < 0.01$ , \*\*\* =  $p < 0.001$  when compared to vehicle by two-way ANOVA with bonferroni post hoc test. Data expressed as mean  $\pm$  SEM. N=5. (B) In the presence of 200 nM oxytocin. \*\*\* =  $p < 0.001$  when compared to vehicle by two-way ANOVA with bonferroni post hoc test. Data expressed as mean  $\pm$  SEM. N=5.

*“REPROCELL's unique capabilities enabled us to generate important data on the safety of the Dapivirine Vaginal Ring for women's HIV prevention.”*

— Jeremy Nuttall, IPM

## References

- IPM [The dapivirine ring](#). IPM (2020)
- IPM [A long acting ring for women's HIV prevention](#). IPM (2020)
- IPM [The monthly dapivirine ring: frequently asked questions](#). IPM (2020)