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Background

Vaginal Microbicides are a women-controlled method to reduce or block the transmission of HIV and other STIs. Several microbicide prototypes are in the clinical trial pipeline but no products have been commercialized to date. Lack of patient compliance has been shown to impair the real world effectiveness, so it is important to understand women's preferences while designing these products.

We are investigating carrageenan-based microbicide prototypes in the form of gel ovules which when inserted vaginally will function as drug delivery vehicles. To understand how women's preferences and willingness to use are governed by the product's physical attributes, we have prepared gel ovules of varying size, shape and firmness in an iterative design process.

Iterative Design process

Focus groups

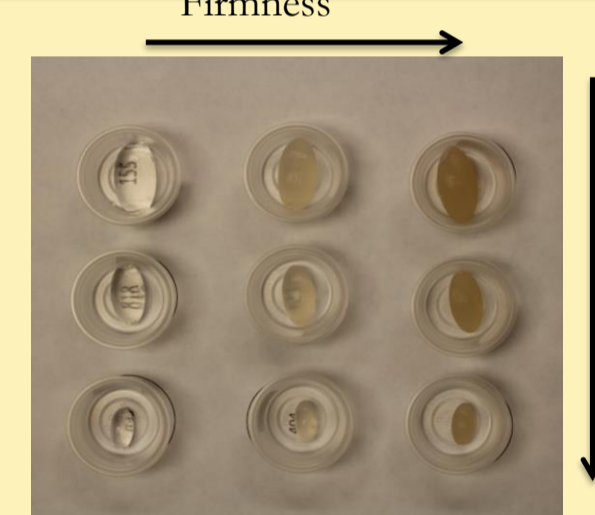
Samples: 3 sizes, 4 shapes and 5 firmness levels
Preferred shape: Long oval
Preferred size: Variable 1-5 mL, Preferred firmness: Variable



Zaveri T, Powell K.A, Li B, Ziegler G.R, Hayes J.E. Improving Acceptability of Vaginal Drug Delivery System by using Sensory Methods. Society of Sensory Professionals Conference, October 2012, Jersey City, NJ.

Sensory test for size and firmness

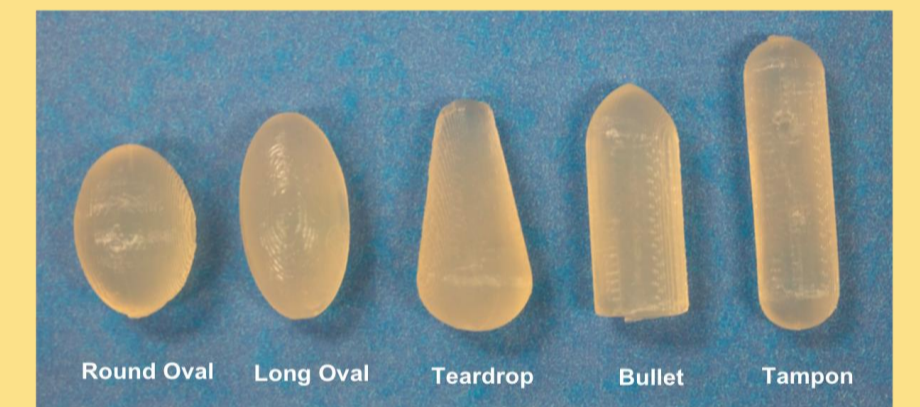
Sample shape: Long oval
Preferred firmness: $G' = 25000$ Pa (w/o applicator), 12500 Pa (with applicator)
Preferred size: 3 mL



Li B, Zaveri T, Ziegler G.R, Hayes J.E. User preferences for a carrageenan-based vaginal drug delivery system. PLoS ONE 8(1): e54975 (2013)

Sensory test for second generation of shapes

Sample firmness: $G' = 25000$ Pa
Sample size: 3 mL
Preferred shape: Long oval and bullet



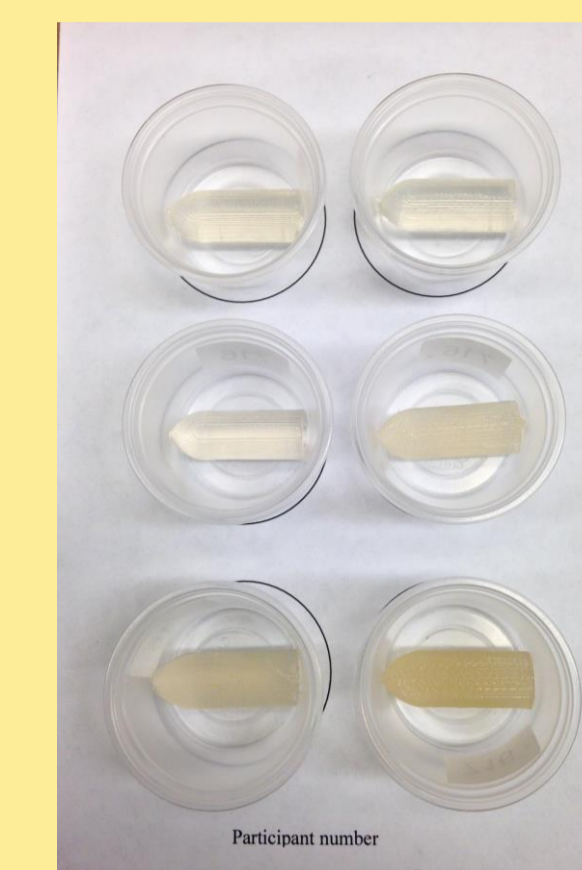
Li B, Zaveri T, Ziegler G.R, Hayes J.E. 2013. Shape of vaginal suppositories affects willingness-to-try and preference. Antiviral Research; 97(3): 280-4 (2013)

Firmness can also be divided into sub-qualities of feeling of hardness (storage modulus G') and elongation properties (degree to which it can be stretched/compressed before breaking). **In the present study, we explored how small and large scale deformation properties may interact to influence preference and willingness to try in sexually active women.**

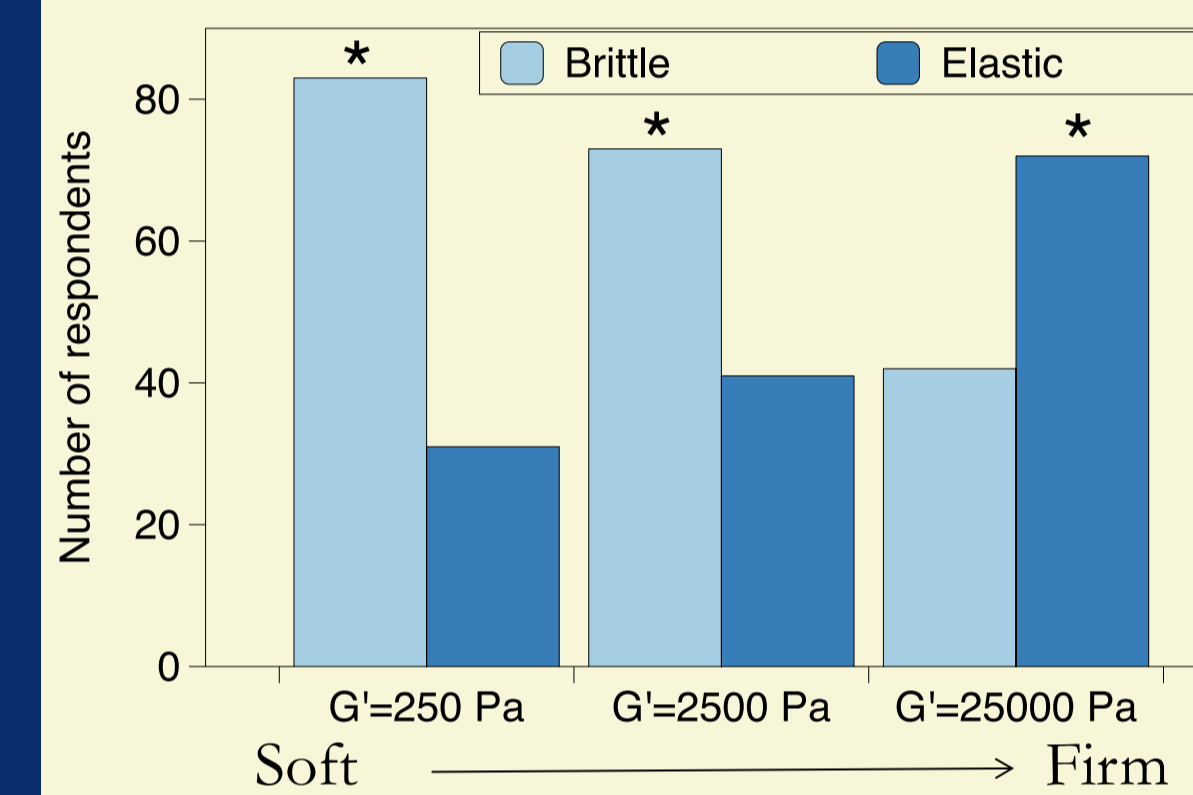
Methods and Results: Sensory Evaluation

Ex-vivo CLT 1

Pairs of brittle and elastic samples at $G' = 250$ Pa, 2500 Pa, 25000 Pa



Forced choice preference task followed by open comment box to give reasons for preference



"soft yet firm, feels as though [it] would be easily placed" and "just right amount of firmness and flexibility"
Comments for elastic gel with $G' = 25000$ Pa

Small and large-scale deformation properties of gels interact: at lower G' women prefer brittle (less elastic) suppositories, but at high G' the more elastic suppositories are preferred.

Vaginal Products	Number of users
Vaginal contraceptive products such as Nuvaring	5
Spermicidal gels and films	3
Yeast infection medicines such as Vagisil and Monistat	26
Douche	5
Menstruation products such as tampons	71
Lubrication products such as KY gels, liquibeads and Vitamin-E suppositories	39

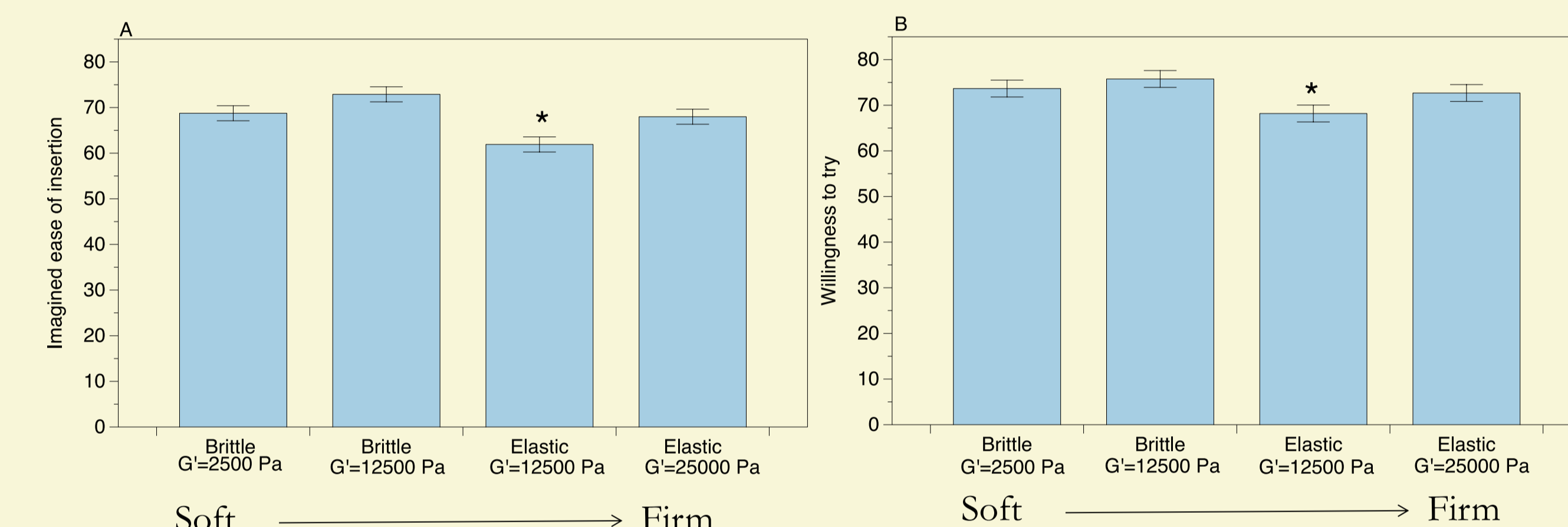
No significant associations found for brittle versus elastic preference for users versus non users of common vaginal products.

Ex-vivo CLT 2

Samples: $G' = 2500$ (Brittle) $G' = 12500$ (Brittle & Elastic), $G' = 25000$ (Elastic)



Imagined ease of insertion
Not at all easy ————— Very easy
Willingness to try
Not at all willing ————— Very willing
Arrange the samples in order of preference

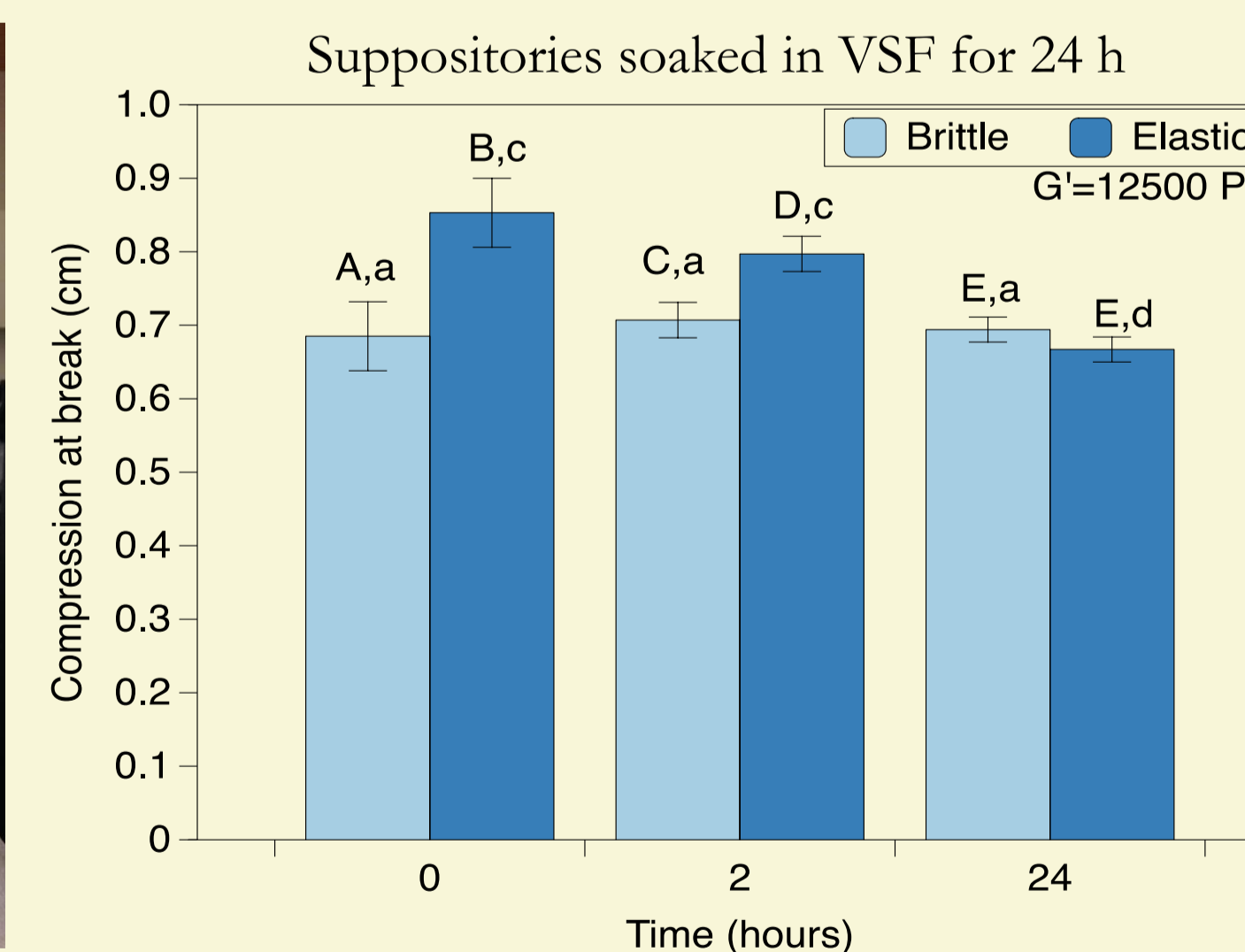
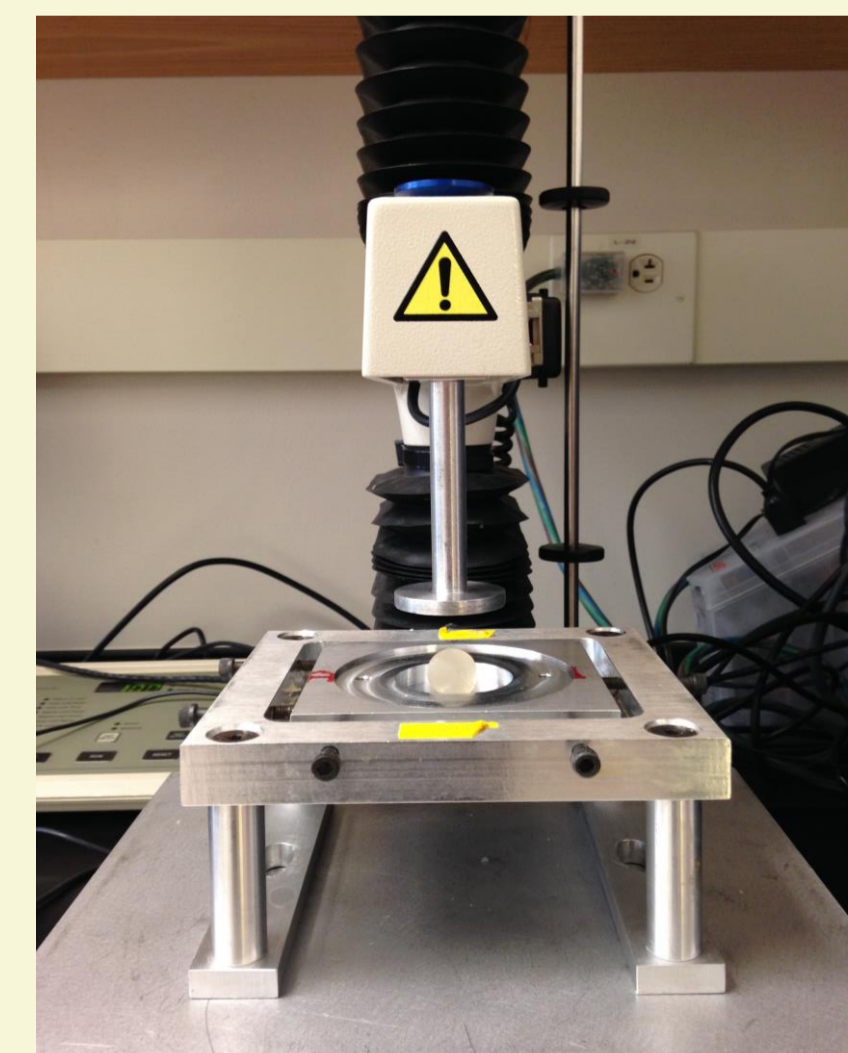
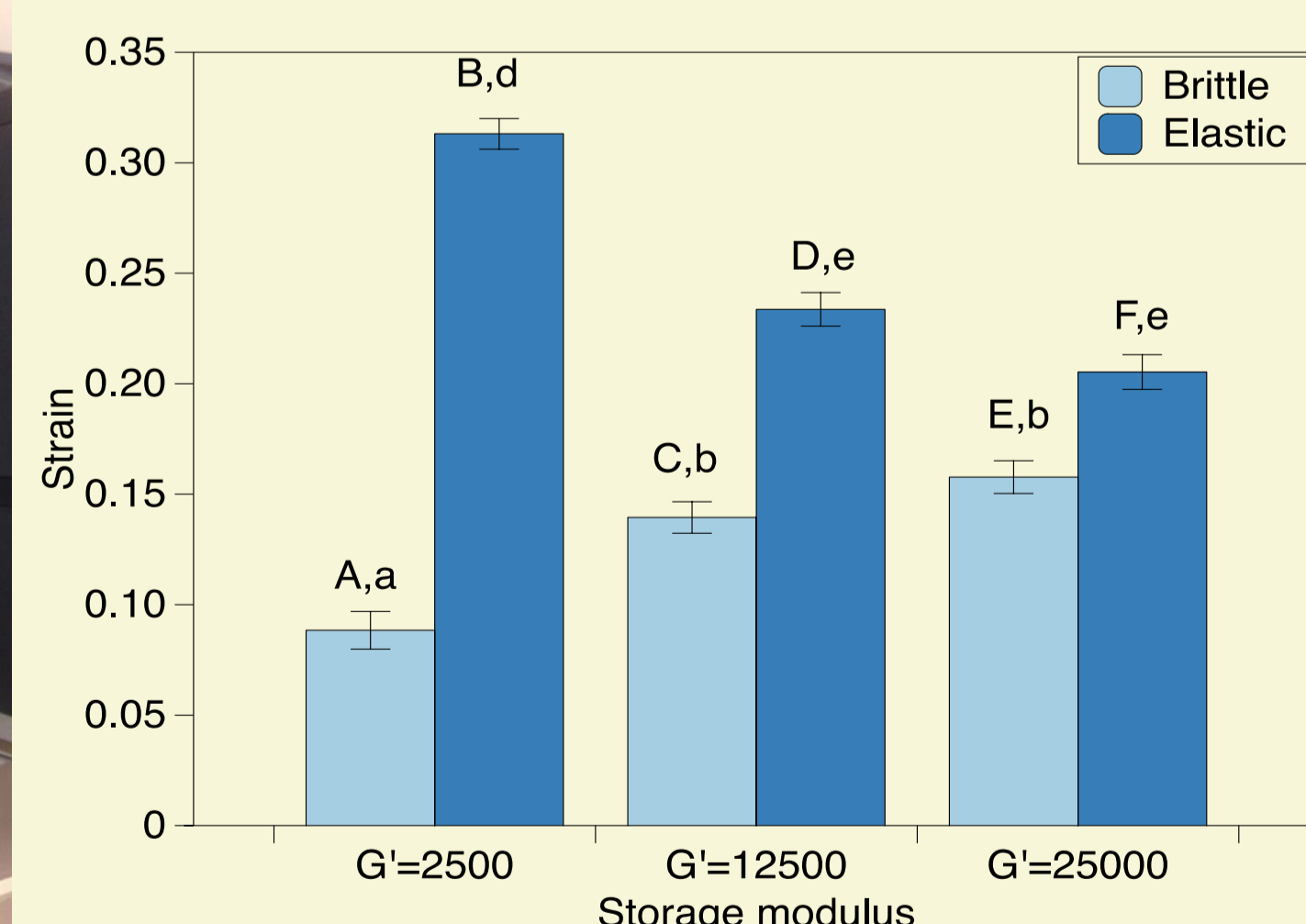
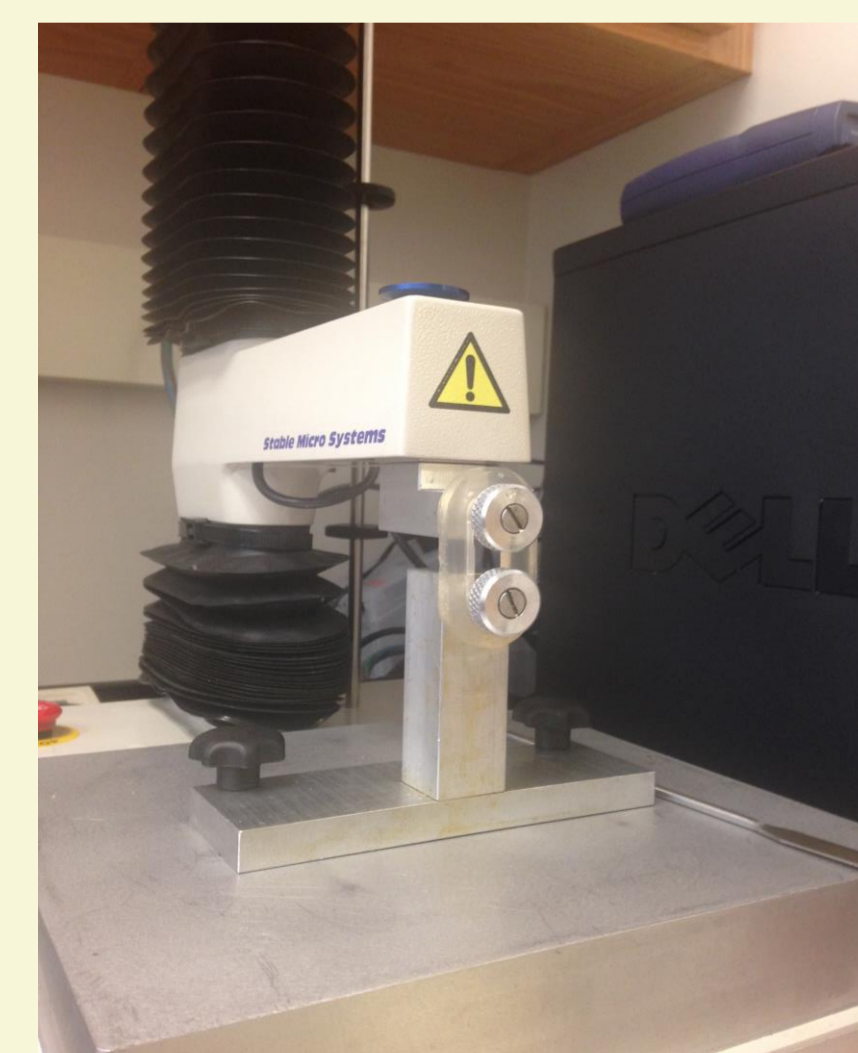


Asterisks (*) indicate a significant difference at $\alpha = 0.05$ (Tukey's Honest Significant Difference (HSD)).

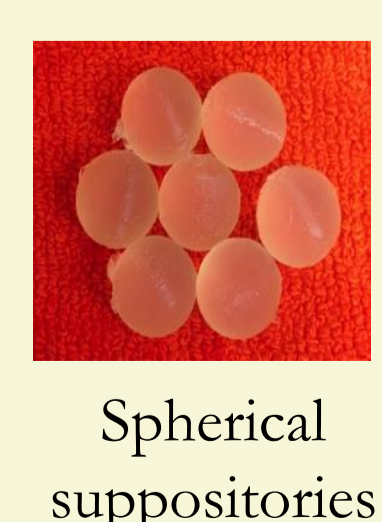
Rank Order	1	2	3	4	Borda Counts
Brittle ($G' = 12500$)	40	34	30	16	218
Brittle ($G' = 2500$)	40	34	24	22	212
Elastic ($G' = 25000$)	22	31	43	24	171
Elastic ($G' = 12500$)	18	21	23	58	119

Brittle suppositories at $G' = 12500$ Pa most preferred.

Methods & Results: Physical characterization and drug release



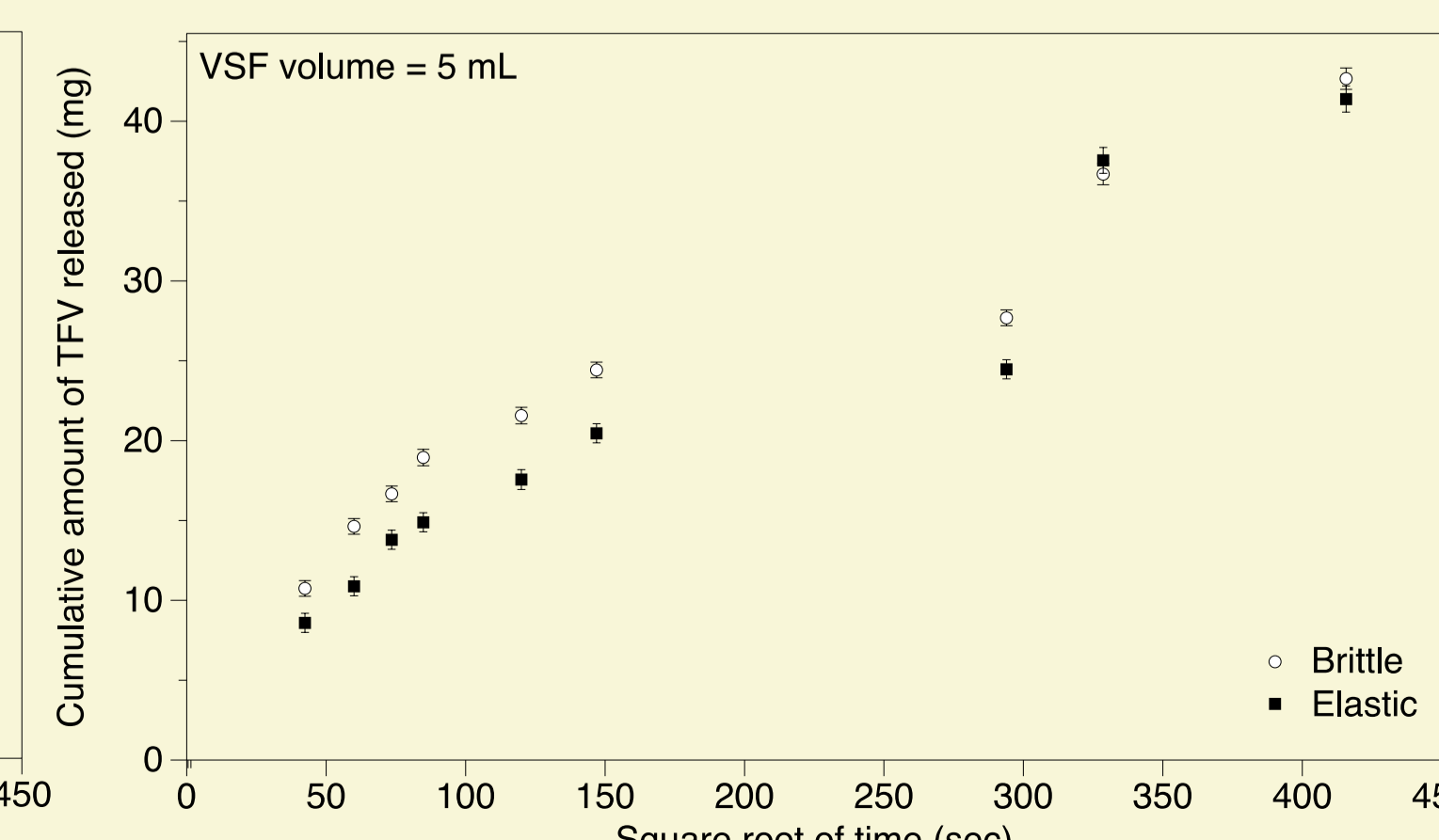
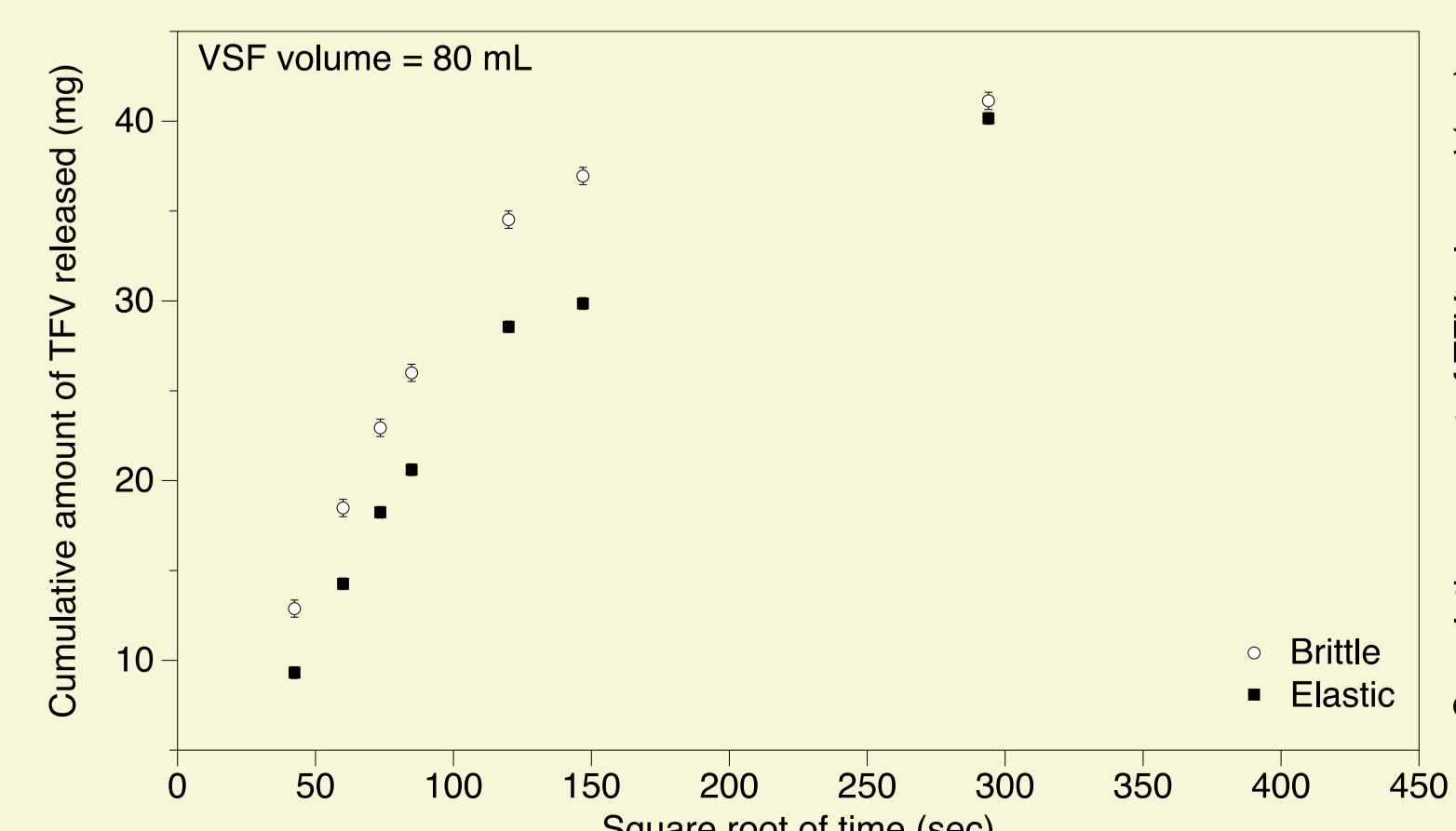
Elastic gels can withstand more strain in tension and compression compared to brittle gels before fracturing.



Spherical suppositories



Measure release of antiviral drug Tenofovir (TFV) over 48 hours in Vaginal simulant fluid (VSF)



Drug is released at a significantly slower rate from elastic suppositories as compared to brittle suppositories.

Conclusions

- Previous work has shown that multiple factors influence women's willingness to try vaginal microbicides. These include sensory attributes, like size, shape and firmness, as well as non-sensory factors like the frequency of application, duration of protection and potential for covert use.
- In this iterative design process, we have further explored the physical parameter of firmness by creating gels with the same small strain measurements but with different large strain attributes.
- Small strain measurements i.e. G' typically relates to perception of "firmness" and influence the imagined comfort of the suppository during insertion and use. On the other hand large strain attributes which quantify the failure properties, i.e. how much force or deformation is required to break the material are related to the amount of manipulation that the suppository could survive during insertion.
- Women perceive both suppository types very differently (depending on G') in terms of its sturdiness, ease of handling, imagined ease of insertion which in turn affects their preferences as well as willingness to use.
- A range of instrumental measures need to be combined with sensory data for product development.
- Incorporating women's opinion during the initial stages of product development will result in a product design that women prefer hence, ensuring better user compliance especially for critical applications such as prevention of HIV transmission.

Acknowledgements

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