



Short Communication

Shape of vaginal suppositories affects *willingness-to-try* and preferenceBangde Li ^{a,b}, Toral Zaveri ^{a,b}, Gregory R. Ziegler ^b, John E. Hayes ^{a,b,*}^a *Sensory Evaluation Center, College of Agricultural Sciences, The Pennsylvania State University, University Park, PA, USA*^b *Department of Food Science, College of Agricultural Sciences, The Pennsylvania State University, University Park, PA, USA*

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ABSTRACT

HIV and other sexually transmitted infections (STIs) are a global threat to public health that may be countered, in part, by microbicides. A successful microbicide must be both biologically efficacious and highly acceptable to users. Sensory attributes have a direct influence on product acceptability. We created a series of vaginal suppositories appropriate for use as microbicides to investigate the influence of shape on women's *willingness-to-try*. The influence of perceived size and firmness on acceptability was also assessed.

Sexually-active women ($n = 99$) were invited to participate in an evaluation of vaginal suppositories in 5 different shapes including: Bullet, Long Oval, Round Oval, Teardrop and Tampon. The volume (3 mL) and formulation for these five prototypes were identical. After manipulating prototypes *ex vivo* (in their hands), participants rated their *willingness-to-try* on a 100-point visual analog scale. The appropriateness of size and firmness were evaluated using 5-point just-about-right (JAR) scales. Each participant evaluated all five prototypes individually. Samples were presented in a counterbalanced monadic sequence using a Williams design.

Mean *willingness-to-try* varied by shape, with Bullet and Long Oval receiving significantly higher scores. This was consistent with JAR data for size, as 70% and 65% of women indicated these shapes were 'just-about-right', respectively. In contrast, a minority of women endorsed the other 3 shapes as having a size that was 'just-about-right'. The proportion of women who felt the firmness was 'just-about-right' was uniformly high, irrespective of shape, suggesting prior attempts to optimize the formula were successful. Perceptions of size and firmness were influenced by the physical length and width of the prototypes, in spite of having constant volume. Women showed high *willingness-to-try* when asked to assume they were at risk. These results are relevant for behavioral and formulation scientists working on microbicides, to better understand the influence of sensory attributes on acceptability, as acceptability and compliance ultimately impact effectiveness.

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HIV and other sexually transmitted infections (STIs) are a global threat to health; in spite of current prevention efforts, there were 2.7 million new infections world-wide in 2010 (UNAIDS, 2011). Topical microbicides are a promising solution, as they empower women to protect themselves (Morrow et al., 2007; Stone, 2002). More than 50 microbicide candidates are under development (AMD, 2009). A successful microbicide must be biologically efficacious and highly acceptable to users (Elias and Coggins, 2001; Mantell et al., 2005; Severy et al., 2005). Acceptability impacts user adherence to microbicide use and thus real world effectiveness (Abdool Karim et al., 2010; Masse et al., 2009; Nel et al., 2011). User acceptability must be considered along with pharmacokinetic-

ics and toxicity if efficacious prototypes from controlled trials are to be effective in the field (Morrow and Hendrix, 2010).

Microbicide acceptability involves myriad factors, including user characteristics, context, and product attributes (Morrow and Hendrix, 2010). At the pre-clinical level, microbicide characteristics are critical for product acceptability (Morrow and Ruiz, 2008); colorless and odorless microbicide gels may be more appealing (Morrow et al., 2003). Lubrication may be a positive feature of microbicides (Whitehead et al., 2006), although sexual pleasure may be reduced due to the messiness from a microbicide gel (Giguere et al., 2012). Perceptual attributes (e.g. ropiness, graininess, and slipperiness) that are best quantified with human assessors (Mahan et al., 2011) may also be important. Indeed, sensory attributes may critically influence user acceptability, but their effects have not been well investigated.

In the packaged goods industries, the influence of sensory attributes on acceptability is frequently assessed with just-about-right (JAR) scales (Popper and Kroll, 2005; Rothman and Parker, 2009). A

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JAR scale is a bipolar instrument with semantic anchors at each end, reflecting appropriateness of a low and high intensity, respectively. The midpoint is labeled 'just-about-right', indicating this attribute is at an appropriate level in the product. According to American Society of Testing and Materials guidelines, most researchers use five categories (e.g. 'much too small', 'somewhat too small', 'just about right', 'somewhat too big', and 'much too big') (Rothman and Parker, 2009). Hedonic and intensity scales are typically used separately, but JAR scales intentionally combine these two measurements to assess attribute appropriateness (Stone and Sidel, 2004); attribute quality is evaluated relative to a theoretical ideal. JAR scales are popular for product reformulation or optimization (Xiong and Meullenet, 2006) because they are easy to use and generate actionable data. Practically, attempts are made to improve an attribute when more than 20% of the responses are 'too-little or 'too-much' (Meullenet et al., 2007).

In previous qualitative research, most women (45 of 57) preferred semisoft ovoids over spheres or teardrops, but preferences for size and firmness were less clear (Zaveri et al., 2012). Consequently, we conducted a larger quantitative study on oval prototypes using a factorial design and response surface modeling, identifying an optimum near 3 g and firmness (G') of 25 kPa (Li et al., 2013). As part of an iterative optimization process, the current study investigated a second generation of suppository shapes at constant physical firmness and volume.

We investigated the effect of shape on *willingness-to-try*, and perceived appropriateness of size (*size*) and firmness (*firmness*). Shapes included Round Oval, Long Oval, Teardrop, Bullet and Tampon (Fig. 1). These names are provided for readability and discussion; they were never used with participants, who referred to samples using random 3-digit codes.

Women ($n = 99$) were recruited as described elsewhere (Li et al., 2013) to evaluate prototypes *ex vivo* (in their hands) at the Sensory Evaluation Center at Penn State. All procedures were approved by the local Institutional Review Board (protocol #36943). Participants reported race and ethnicity using categories in OMB Directive 15. Most were married, college-educated white women; complete demographics are provided in *Supplemental Table 1*, and vaginal product usage is summarized in *Table 1*. Of the 99 participants, 37 had participated in our previous microbicide studies.

Participants watched a short video about the product concept in our waiting room, which described how to evaluate a prototype: (1) take the sample and put it into her non-dominant hand; (2) gently stroke the sample with the index finger of her dominant hand; (3) put the sample between her fingers and pinch gently

Table 1
Product usage.

Products	Usage (%)
Menstruation products, such as tampons	64
Lubrication products such as KY® gels, liquibeads and vitamin-E suppositories	37
Yeast infection medicines, such as Vagisil® and Monistat®	28
Douche	8
Vaginal contraceptive products, such as Nuvaring®	4
Spermicidal gels and films	2
Decline to answer	9

(hand not specified; shown as dominant hand in video); (4) finally hold the sample between her fingers and imagine she was trying to insert the sample into her vagina (hand not specified or shown). After watching the video, women deciding to participate provided written informed consent before entering individual test booths. Participants were reimbursed for their time.

Women rated *willingness-to-try* using a 100-point visual analog scale. Women were told these products would be used without an applicator. Sample presentation was counterbalanced in a Williams design. To avoid low *willingness-to-try* ratings due to low perceived STI risk, women were asked to assume they might need these products "to prevent potential infections, including Chlamydia, herpes and HIV". Appropriateness of size and firmness were assessed using 5-point categorical just-about-right (JAR) scales. (Here forward, we use *size* and *firmness*, in italics, to refer to appropriateness scores for these attributes). JAR is a global approach; specific contexts (e.g. insertion versus coitus) were not provided. Women ranked the shapes from most to least preferred after all samples had been evaluated. Demographics were collected at the end of the test.

Data were collected using Compusense Five v5.2 (Guelph, Ontario) and analyzed in JMP v9.0.2 (Cary, NC). Whether shape influenced *willingness-to-try* was tested via ANOVA, with participant as a random effect and shape as a fixed effect. Tukey's Honest Significant Difference was used for post hoc comparisons. Response distributions within a JAR scale category were compared using the Cochran–Mantel–Haenszel (CMH) test (Rothman and Parker, 2009). Exponential regressions characterized relationships between physical characteristics and percentage of "too-big" and "too-firm" responses using DataGraph v3.0 (Chapel Hill, NC). Ranking was analyzed via Friedman's test; rank-sums were calculated

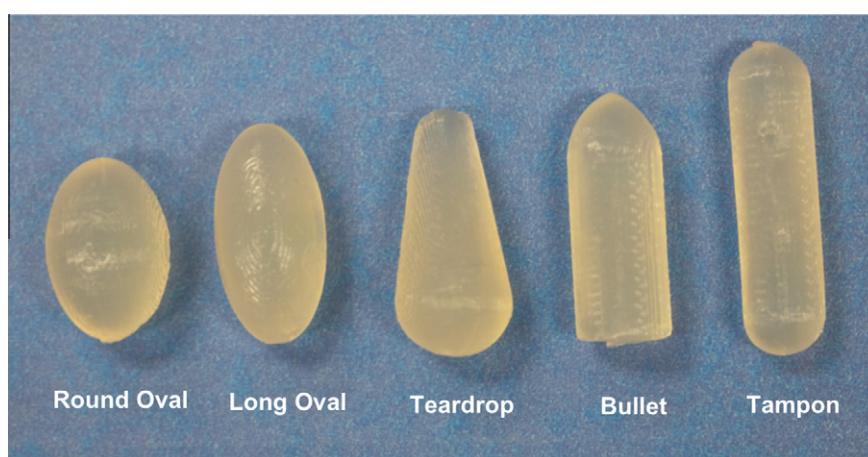


Fig. 1. Second generation microbicide prototypes. Volume is constant at 3 mL across all five shapes. Samples were prepared with kappa carrageenan, potassium chloride and water 1 day before evaluation, and stored in 1-oz transparent plastic cups at 16 °C with the lids tightly sealed until evaluation.

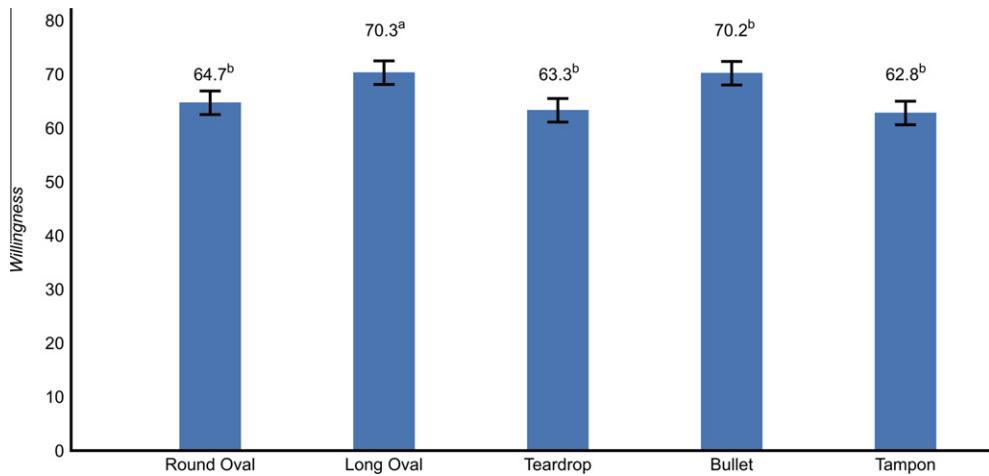


Fig. 2. Effect of Shape on *willingness-to-try*, which was measured on a 100 point visual analog scale. Indented semantic anchors at 10 ('not at all willing') and 90 ('extremely willing') were provided to minimize end avoidance bias. Means with different letters indicate a significant difference at $\alpha = 0.05$ (Tukey's HSD).

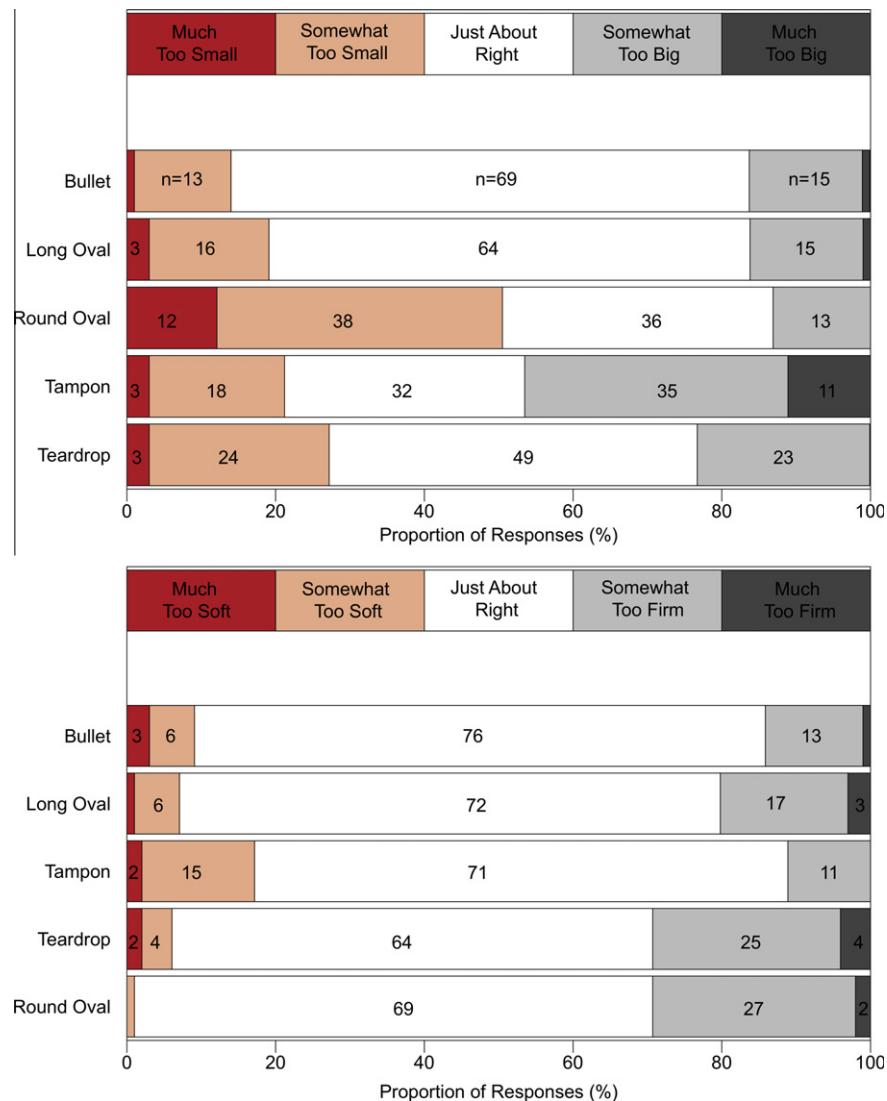


Fig. 3. Distributions of responses for size (top) and firmness (bottom). X-axis is the proportion of responses for each category on the just-about-right scale for size. Numbers inside the bars are the raw number of participants endorsing that category.

and compared using least-significant-differences (Lawless and Heymann, 2010).

Willingness-to-try values differed by shape ($F_{4,392} = 6.99$, $p < 0.001$); shape explained 67.5% of the variance. Long Oval and Bullet had significantly higher willingness-to-try than the other shapes, but were not significantly different from each other (Fig. 2). There were no significant differences between Round Oval, Teardrop and Tampon. These data confirm prior qualitative work (Zaveri et al., 2012) quantitatively, and document the differential acceptability of second-generation shapes (Bullet versus Tampon).

All five shapes had mean willingness-to-try scores above 50 (the scale midpoint). This indicates our iterative optimization produced generally acceptable prototypes, and suggests participants would be willing to try these microbicides if they were functional and needed. Women have expressed a strong desire to try microbicide gels for preventing STIs whether they were at risk or not (Carballo-Diequez et al., 2012; Ramjee et al., 2007; Ventuneac et al., 2010). Participants were explicitly informed these prototypes were intended to prevent transmission of diseases like Chlamydia, herpes and HIV, and that they should evaluate the product assuming they might need such a product to avoid potential 'othering', as qualitative interviews (Zaveri, unpublished data) had indicated some women felt they would not need or use these types of products due to low perceived risk.

Regarding size, there was large variability in the endorsements of 'just-about-right', and the distribution of responses were significantly different ($\chi^2_8 = 100.26$, $p < 0.001$) across shape (Fig. 3, top), in spite of having an identical volume and mass (3 g). For the Long Oval and Bullet, most participants endorsed just-about-right, consistent with greater willingness-to-try scores. Conversely, the Round Oval distribution was skewed toward too small, and the Tampon distribution was skewed toward too big. The Teardrop distribution was not skewed, but was broader than for Long Oval or Bullet, as fewer women thought it was just-about-right. Since all prototypes were the same volume and mass, the effect of shape on size was a difference in perception, rather than actual physical size.

To explore this further, we plotted the proportion of participant responses for 'too big' against the measured length of the prototype (Fig. 4, top). The longer the prototype, the greater the number of women who thought it was 'too big' ($R^2 = 95.1\%$), suggesting a relationship between perceived size and physical length. (However, panelists did not assess size; instead, they judged the appropriateness of the size, a subtle but important distinction.) Our finding is consistent with work showing that product and container shapes effect volume perception (e.g. taller glasses are perceived as being larger than shorter ones (Raghbir and Krishna, 1999; Wansink and Van Ittersum, 2003)).

Prototype firmness appeared appropriate, evidenced by greater than 65% of just-about-right responses. The proportion of just-about-right endorsements should be uniformly high, if our previous optimization (Li et al., 2013) was successful. However, the proportions at the extremes ('too soft' v. 'too firm') did vary as a function of shape ($\chi^2_8 = 41.59$, $p < 0.001$). Bullet received the highest proportion of just-about-right endorsements, and most women also reported the Long Oval and Tampon were just-about-right for firmness, though they had slightly broader distributions. Teardrop and Round Oval distributions were skewed toward 'too firm'; 29% of women found them too firm, although a majority still felt their firmness was just-about-right.

As with size, we believe the differing firmness, despite a constant formulation, is evidence of a perceptual bias related to the shape. To explore this further, we plotted the proportion of participant responses for 'too firm' against the physical width of the prototype (Fig. 4, bottom), and as width increased, the proportion of women who thought it was too firm increased ($R^2 = 96.0\%$). The width of

Teardrop was taken at the widest point, as we had informally observed most women grasp it at the larger end (Zaveri, unpublished data). Thus, it seems a thicker cross section appears to make the product seem firmer.

Rankings across the five prototypes were significantly different ($\chi^2_4 = 50.02$, $p < 0.0001$). Bullet and Long Oval had higher Friedman rank-sums than the other three shapes, but their rank-sums were not significantly different from each other (Supplemental Fig. 1). Nor were the remaining shapes different from each other, consistent with the willingness-to-try data. Additional insight is gained from the ranking place distributions (Supplemental Table 2). While Tampon rank-sum was not significantly lower than the rank-sums for Round Oval or Teardrop, the Tampon shape was clearly inferior, as it was the last choice for 42% of the respondents. For comparison, Round Oval was the last choice for 29% of the respondents, Tear Drop 22%, and Long Oval and Bullet were 3% each.

In summary, we show that simple changes in the shape of a vaginal suppository influences a woman's willingness-to-try. We extend our previous results to a second generation of prototypes, identifying other shapes that are more preferred by women. One limitation is the use of *ex vivo* evaluation to measure acceptability; it is quite possible antiviral delivery systems with a high acceptability in the hand may still be unacceptable when used vaginally. However, it is also true that poor *ex vivo* acceptability may cause failure if women are unwilling to try the microbicide. Thus,

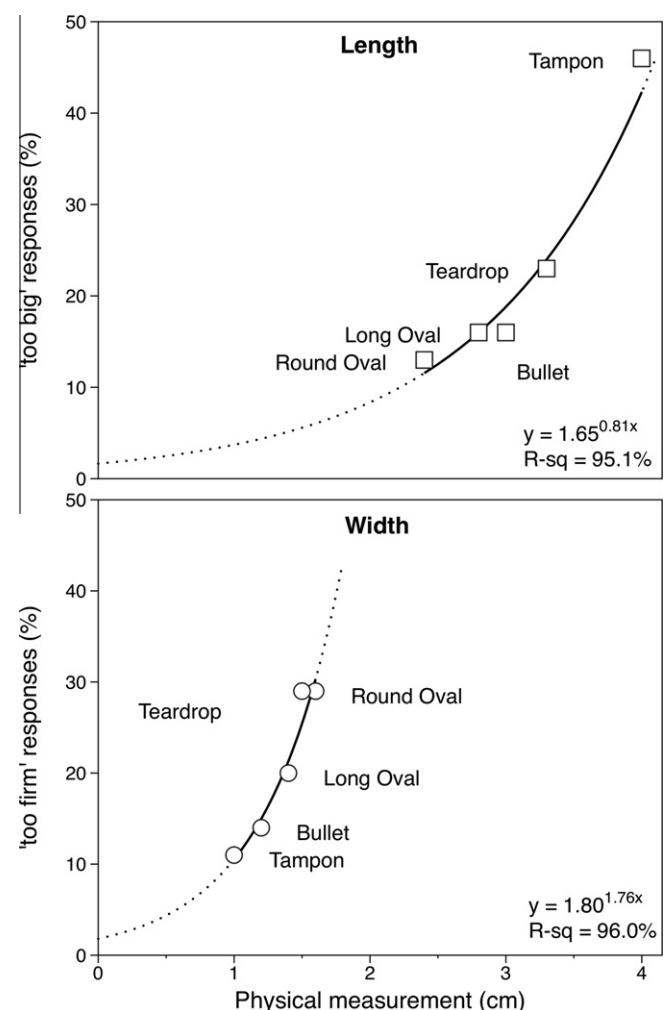


Fig. 4. Relationship between physical measurement and 'too big' or 'too firm' responses.

ex vivo testing can serve as a rapid, inexpensive screen prior to expensive toxicology studies in animals and clinical trials in humans. Present data indicate Bullet and Long Oval shapes are good candidates for further development. Surprisingly, a familiar shape like Tampon was clearly inferior; our data suggest it might be due to perceived size, although we cannot rule out prior association with menstruation.

We also show that shape strongly influences women's thoughts about the appropriateness of size and firmness, even when volume and formulation are held constant. This is a critical insight that can be leveraged by behavioral and formulation scientists working on microbicides. For example, if a specific volume is required for effective coating and drug delivery, this can be balanced against user perceptions of efficacy (too small) or willingness-to-use (too big) by manipulating the product shape.

Finally, these data support the view that standard sensory science methods for optimizing products can be useful in assessing microbicide acceptability. Our goal here is to adapt existing tools to speed up antiviral microbicide development through the early elimination of delivery systems that are non-starters. While sensory attributes presumably influence acceptability, acceptability and adherence are not synonymous, as acceptability can be defined as factors that potentially influence adherence, within a broader social and cultural context (Mensch et al., 2012). Thus, approaches used here are meant to complement intravaginal testing, and not replace it.

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Appendix A. Supplementary data

Supplementary data associated with this article can be found, in the online version, at <http://dx.doi.org/10.1016/j.antiviral.2012.12.024>.

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