

# A Double-Blind, Placebo-Controlled, 2-Way Crossover Study Using Thermography to Assess the Pharmacodynamics of Sildenafil Cream, 3.6% in Healthy Women



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## Introduction

**Sildenafil Cream**, 3.6% is a novel topical formulation in Phase 2 clinical development for the treatment of Female Sexual Arousal Disorder (FSAD). **FSAD** is characterized by decreased clitoral and labial sensation, reduced genital engorgement and diminished vaginal lubrication, **Research** to date has provided substantial evidence supporting the role of the NO-cGMP smooth muscle mediated vasodilatory pathway in the female sexual arousal response, advocating for the continued investigation of Sildenafil Cream, 3.6% as a first-in-class therapy for FSAD.

## Aims

**1)** To evaluate the feasibility of thermography to assess the pharmacodynamics of Sildenafil Cream, 3.6% and **2)** to evaluate the preliminary efficacy of Sildenafil Cream, 3.6% using thermography to assess genital blood flow and the Sexual Arousal Questionnaire to assess self-reported measures of sexual arousal in healthy women.

## Methods

### Participants

**Six** women aged 25 to 55 without sexual dysfunction were recruited to participate (*M* age= 36.3 years). All participants passed a detailed medical screening at Session 1 in order to be eligible for the 2-way crossover design for Sessions 2 & 3.

### Stimuli

Different audio-visual stimuli were shown in each of the three sessions including **neutral** baseline travelogues for temperature stabilization, and **sexually explicit** films for inducing sexual response.

### Measurement Tools

Genital and thigh temperature (non-genital control) were remotely recorded during each session using a FLIR system Thermos-Vision A320 **thermal imaging camera** and FLIR Research IR v4.4 software (FLIR Systems, Inc, N. Billerica, MA, USA)

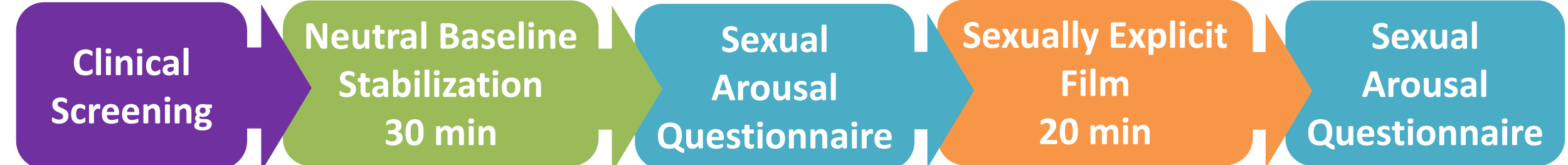
**Self-report measures** of cognitive arousal and perception of genital change were also obtained after each film using Likert-style questions adapted from previous research and the SFQ-28 arousal sensation and lubrication domain.

## Methods (continued)

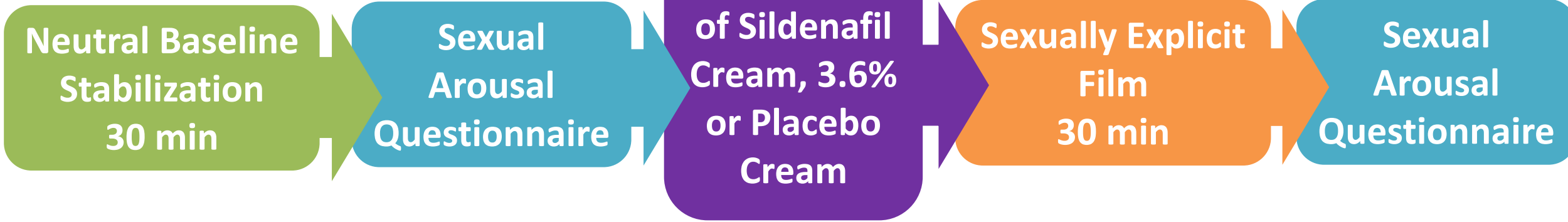
### Study Design

This was a Phase 1, double-blind, placebo-controlled, crossover study where participants attended a first session to establish eligibility and then were randomly assigned to receive an application of **placebo cream** or **Sildenafil Cream, 3.6%** at Session 2 and Session 3 (separated by a 4-8 day washout period).

### Session 1



### Sessions 2 & 3

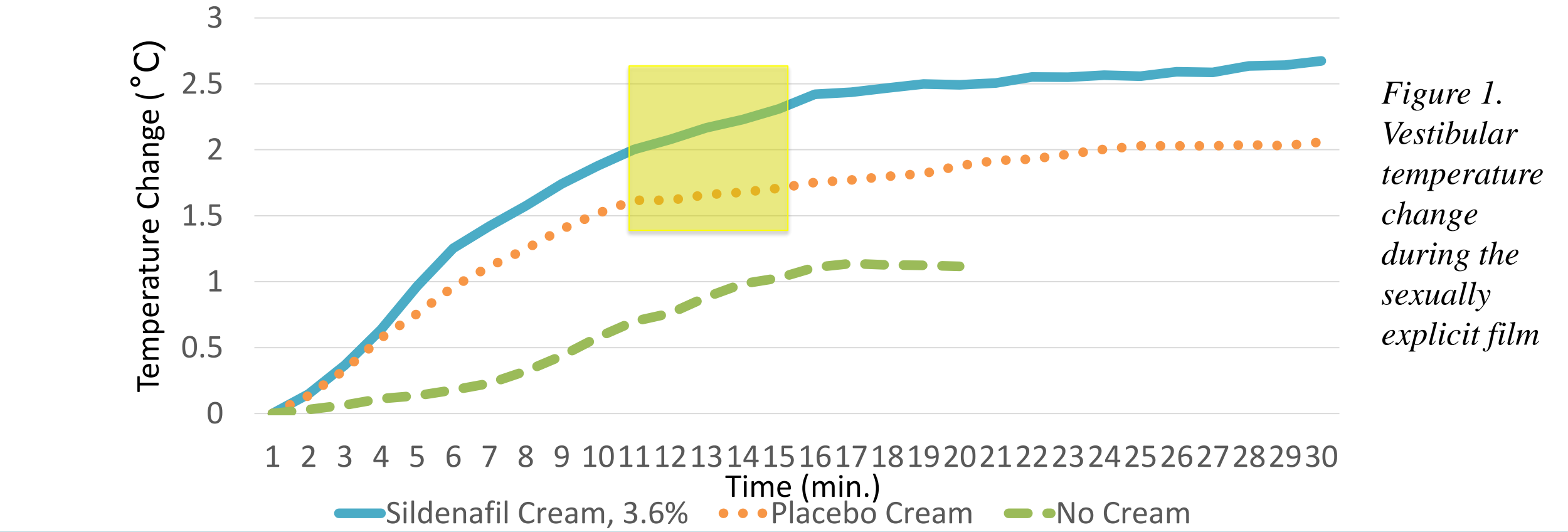


## Results

Temperature data was analyzed using Repeated Measures ANOVAs with time in minutes as the repeated measure and cream condition as the independent variable.

**Manipulation Checks:** There were no significant differences in thigh temperature or baseline genital temperature between the no cream, placebo cream and Sildenafil Cream, 3.6% conditions (all *p* > .10)

**Physiological Sexual Response:** There were statistically **significant** differences between the Sildenafil Cream, 3.6% and placebo cream ( $F(29, 290)=1.58, p=.03, \eta_p^2=.14$ ) as well as the no cream ( $F(19,190)=1.85, p=.02, \eta_p^2=.16$ ) conditions in the vestibule during the sexually explicit film.



## Results (continued)

Statistically **significant** differences were also found in clitoral temperature during the sexually explicit film (vs. placebo cream:  $F(29, 290)=1.50, p=.05, \eta_p^2=.13$ ; vs. no cream:  $F(19,190)=4.47, p=.000, \eta_p^2=.31$ ).

### Onset of Action:

Sildenafil Cream, 3.6% produced a statistically significant **greater linear slope** during minutes 11-15 of the sexually explicit film as compared to the placebo cream for the vestibule (see highlight in Figure 1;  $F(1,10)=7.70, p=0.02, \eta_p^2=.44$ ) and clitoris ( $F(1,10)=5.69, p=.04, \eta_p^2=.36$ ).

### Self-Report Measures of Arousal:

A MANOVA on measures of self-reported arousal demonstrated statistically significant differences between the Sildenafil Cream, 3.6% and placebo conditions.

Table 1. Mean (sd) arousal ratings following the sexually explicit stimulus

Sexual Arousal Rating	Sildenafil Cream, 3.6%	Placebo Cream	p value
Overall Sexual Arousal	8.17 (1.17)	7.50 (.55)	.24
Peak Sexual Arousal	8.50 (.84)	7.50 (.55)	.03
Mental Sexual Arousal	8.33 (1.21)	7.00 (1.10)	.07
Feel like having sex with partner	9.17 (.75)	7.50 (1.20)	.02
Feel like masturbating	8.50 (1.38)	7.17 (1.33)	.12
Physical Sexual Arousal	8.33 (1.21)	7.50 (1.05)	.23
Sexual arousal comparison to partner	1.17 (2.14)	.50 (1.64)	.56

A chi-square analysis showed that participants reported **more** genital lubrication in the Sildenafil Cream, 3.6% condition than the placebo conditions  $\chi^2(2)= 6.67, p=.04$

## Conclusion

These results **support** the use of thermography to measure genital temperature following topical cream application and further validated the potential for Sildenafil Cream, 3.6% to be a **promising**, on-demand treatment for FSAD patients.