

The Enhancement of Female Sexual Function with ArginMax, a Nutritional Supplement, Among Women Differing in Menopausal Status

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We conducted a double-blind, placebo-controlled study to determine the role of dietary supplementation on sexual function in women of differing menopausal status. One hundred eight (108) women, age 22–73 years, who reported a lack of sexual desire, enrolled as participants. Of these, 55 received ArginMax for women and 53 received placebo. ArginMax for women contains L-arginine, ginseng, ginkgo, damiana, multivitamins, and minerals. The 108 women, given definitions, self-reported as 59 premenopausal (PRE); 20 perimenopausal (PERI), and 29 postmenopausal (POST). After 4 weeks, PRE women on ArginMax primarily reported significant improvement in level of sexual desire (72%; $p = 0.03$) and satisfaction with overall sex life (68%; $p = 0.007$), compared with placebo group, according to the Female Sexual Function Index (FSFI; Kaplan et al., 1999) scales. Frequency of sexual desire (60%; $p = 0.05$) and frequency of intercourse (56% $p = 0.01$) also increased among the PRE women. In contrast, among PERI women, primary improvements were reported for frequency of intercourse (86%; $p = 0.002$), satisfaction with sexual relationship (79%; $p = 0.03$), and vaginal dryness (64%; $p = 0.03$) compared with placebo group.

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POST women primarily showed an increased in level of sexual desire, with 51% showing improvement, compared with only 8% in the placebo group ($p = 0.008$). Nutritional intervention plays an important role in women's sexual health, but issues and areas of greatest improvement differ among women of different menopausal states. The largest number of attribute improvements were seen in PRE and PERI women, although attribute types vary among these groups. Level of desire was shown to increase significantly in POST women. Since ArginMax for women has been shown to exhibit no estrogen activity, it may be desirable alternative to hormone therapy for sexual concerns.

Sexual function has become a more widely discussed topic in the media and the scientific community since the introduction of sildenafil citrate (Viagra) in 1998. Although sildenafil has demonstrated effectiveness in men with erectile dysfunction, results in women have been mixed (Boyce & Umland, 2001), and the product is not currently recommended for female sexual issues.

There has been a paucity of studies of medications that demonstrate efficacy for women. One study among women, which demonstrated effectiveness for sexual concerns, was a placebo-controlled, double-blind study on a nutritional supplement, ArginMax for women (Ito, Polan, & Trant, 2001). The results from this study demonstrated significant improvements among a wide age range of women (22 to 71 years) in satisfaction with overall sex life, sexual desire, reduced vaginal dryness, and increased frequency of sexual intercourse, orgasm, and clitoral sensation compared with placebo. Because of early trends in age and menopause differences seen in this preliminary study, we recruited more women in the peri- and postmenopausal groups for the present study in order to elucidate these differences.

According to a survey by Laumann, Paik, and Rosen (1999), the incidence of sexual dysfunction in the United States is greater in women (43%) than in men (31%), yet drug therapy for women remains elusive. This survey found that the prevalence of sexual problems tends to decrease with age in women, except for vaginal dryness. They report that nonmarried women are roughly 1–1/2 times more likely to have orgasmic disorders and sexual anxiety than married women (Lauman et al., 1999). Although female sexual disorders are complex and multidimensional in nature, the current study was designed to focus on evaluating the role of nutritional supplementation in female sexual health during different stages of menopause. Both menopausal status and age have been shown to influence the incidence and type of female sexual disorders (Berman et al., 1999; Walsh & Berman, 2004).

MATERIALS AND METHODS

ArginMax for women is a proprietary nutritional supplement that combines L-arginine, Panax ginseng, Ginkgo biloba, and damiana leaf (*Turnera aphrodisiaca*) with vitamins A, C, E, B6, B12, biotin, folate, niacin, pantothenic acid, riboflavin, thiamin and the minerals, calcium, iron, and zinc. L-arginine has been well established as a nitric oxide precursor, and ginseng may upregulate this conversion process (Chen & Lee, 1995). Ginkgo facilitates microvascular circulation involved in sexual arousal mechanisms (Auguet, Delaflotte, Hellegouarch, & Clostre, 1986). Damiana has been shown to affect hormone receptors (Zava, Dollbaum, & Blen, 1998) and reduce anxiety (Kumar & Sharma, 2005).

All participants were enrolled based on their expressed interest in improving their current sexual function. We recruited subjects by placing ads in local newspapers asking for women over age 21 who suffer from lack of sexual desire or who have trouble getting aroused. Twelve enrolled participants had been previously treated for sexual dysfunction. Five had tried testosterone (3 in ArginMax [ARG] group and 2 in placebo [P] group); seven had tried counseling (3 in ARG group, 4 in P group). In addition, 34 women were on hormones, either traditional hormone therapy or birth control pills (18 in ARG group, 16 in P group) but not for sexual issues. Only 7 women who enrolled reported being on antidepressants (3 in ARG and 4 in P group), and 5 stated that they were on blood-pressure medications (2 in ARG and 3 in P group).

One hundred eight (108) study participants, age 22–73, successfully followed and completed the study protocol. The survey instrument was the Female Sexual Function Index (FSFI; Kaplan et al., 1999), a validated questionnaire with multidimensional scales for assessment of sexual function used in the evaluation of sildenafil in women. We collected medical histories, including self-assessment of menopausal status, blood pressure measurements, and FSFI scores, initially and after 4 weeks. Upon enrollment, subjects were randomly assigned ArginMax for women or placebo in a double-blind fashion. Consent forms, advertising copy, subject's Bill of Rights, questionnaires, and investigators' credentials were reviewed and approved by an independent investigational review board. We conducted statistical analyses using student's *t*-test and Bayesian analysis of binomial data.

Of the 108 subjects who completed the test protocol, fifty-five (55) were on ArginMax and fifty three (53) were on placebo (Table 1). The age distributions were similar ($p > 0.05$), with the ArginMax group ranging from 24 to 73 years (mean age 44.4) and the placebo group ranging from 22 to 68 years (mean age 43.1). Participants' self-assessment of menopausal status, after they were given definitions, resulted in 59 women being categorized as premenopausal (PRE), 20 as perimenopausal (PERI), and 29 as postmenopausal

TABLE 1. Number of subjects

Group	Total#	#ArginMax	#Placebo
All	108	55	53
Pre	59	25	34
Peri	20	14	6
Post	29	16	13

(POST). Three of the PERI women and 18 of the POST women were on some form of hormone therapy. Mean ages and ranges for each group are in Table 2.

RESULTS

Summaries of FSFI data in Table 3 demonstrate significant improvements in many parameters among the ARG groups compared with the placebo groups, categorized as PRE, PERI, or POST in menopausal status. The PERI women on ARG reported increased frequency of sex (Q3, 86%, versus 17% on placebo, $p < 0.01$), improved satisfaction with sexual relationship (Q7, 79% versus 33% on placebo, $p = 0.03$), increased satisfaction with overall sex life (Q4, 71%, versus 33% on placebo, $p = 0.06$), increased clitoral sensation (Q9, 71% versus 33% on placebo, $p = 0.06$), and decreased dryness (Q2, 64% versus 17% on placebo; $p = 0.03$). PRE women on ARG improved primarily in satisfaction with overall sex life (Q6, 68% versus 35% on placebo; $p = 0.007$), frequency and level of desire (Q4 and Q5, 60% and 72% versus 38 and 47% on placebo; $p = 0.05$ and $p = 0.03$, respectively), and frequency of intercourse (Q3, 56% versus 26% on placebo; $p = 0.01$). POST women, as a group, increased mainly in level of sexual desire (Q5, 50% versus 8% on placebo; $p = 0.008$) and satisfaction with relationship (Q7, 50% versus 31% on placebo; $p = 0.16$). Also notable in the POST group were the generally lower levels of placebo response, particularly in level of sexual desire (8%).

TABLE 2. Average ages and age ranges

Group	ArginMax		Placebo	
	Mean	Range	Mean	Range
All	44.4	24–73	43.1	22–68
Pre	35.0	24–46	36.1	22–48
Peri	46.9	43–55	47.8	36–57
Post	57.0	42–73	59.5	52–68

* None of the values are significantly different between treatment groups ($p > 0.05$) Student's *t*-test.

TABLE 3. Results from the Female Sexual Function Index (FSFI; Kaplan et al., 1999) for ArginMax versus Placebo

FSFI question	Question								
	1	2	3	4	5	6	7	8	9
ArginMax, PRE: 25 women									
Mean score, start	3.7	3.4	2.8	2.1	1.9	2.0	2.5	3.0	2.9
Mean score, 4 wks	4.1	3.9	3.6	3.1	3.1	3.1	3.5	3.8	3.5
% improved	32%	40%	56%	60%	72%	68%	52%	44%	52%
Placebo, PRE: 34 women									
Mean score, start	3.7	3.1	3.3	2.0	1.8	2.3	2.6	2.7	2.7
Mean score, 4 wks	3.6	3.0	3.4	2.3	2.2	2.6	3.1	3.0	3.0
% improved	24%	29%	26%	38%	47%	35%	35%	29%	38%
p values	0.23	0.20	0.01	0.05	0.03	0.007	0.10	0.13	0.15
ArginMax, PERI: 14 women									
Mean score, start	3.5	2.9	3.2	2.1	1.6	1.9	2.3	2.3	2.3
Mean score, 4 wks	4.4	3.8	4.3	2.7	2.2	2.9	3.5	3.1	3.3
% improved	43%	64%	86%	57%	57%	71%	79%	50%	71%
Placebo, PERI: 6 women									
Mean score, start	4.3	3.5	3.3	1.3	1.3	1.8	2.3	2.2	2.0
Mean score, 4 wks	4.7	3.5	3.0	1.5	1.8	2.3	2.5	2.2	2.2
% improved	17%	17%	17%	33%	50%	33%	33%	17%	33%
p values	0.16	0.03	0.002	0.18	0.38	0.06	0.03	0.10	0.06
ArginMax, POST: 16 women									
mean score, start	2.9	2.3	2.5	2.0	1.8	2.2	2.4	2.2	2.3
Mean score, 4 wks	3.3	2.9	2.9	2.1	2.2	2.7	3.1	2.6	2.7
% improved	19%	25%	38%	31%	50%	44%	50%	31%	38%
Placebo, POST: 13 women									
Mean score, start	2.5	1.6	2.8	1.9	1.7	1.9	2.3	1.5	1.9
Mean score, 4 wks	2.4	1.9	2.8	1.9	1.7	1.9	2.2	1.8	1.9
% improved	15%	15%	31%	23%	8%	31%	31%	31%	15%
p values	0.43	0.29	0.36	0.33	0.008	0.25	0.16	0.50	0.11

Note. Question 1: Over the past 4 weeks how often did you experience discomfort during sexual intercourse?

Question 2 (1 = Almost always, 2 = Most times, 3 = Sometimes, 4 = A few times, 5 = Almost never). Over the past 4 weeks how often did you experience dryness during sexual intercourse? (1 = Almost always, 2 = Most times, 3 = Sometimes, 4 = A few times, 5 = Almost never).

Question 3. Over the past 4 weeks how often did you attempt sexual intercourse? (1 = 0, 2 = 1-2, 3 = 3-4, 4 = 5-6, 5 = 7-10, 6 = 11+).

Question 4. Over the past 4 weeks how often have you felt sexual desire? (1 = Almost never, 2 = A few times, 3 = Sometimes, 4 = Most times, 5 = Almost always).

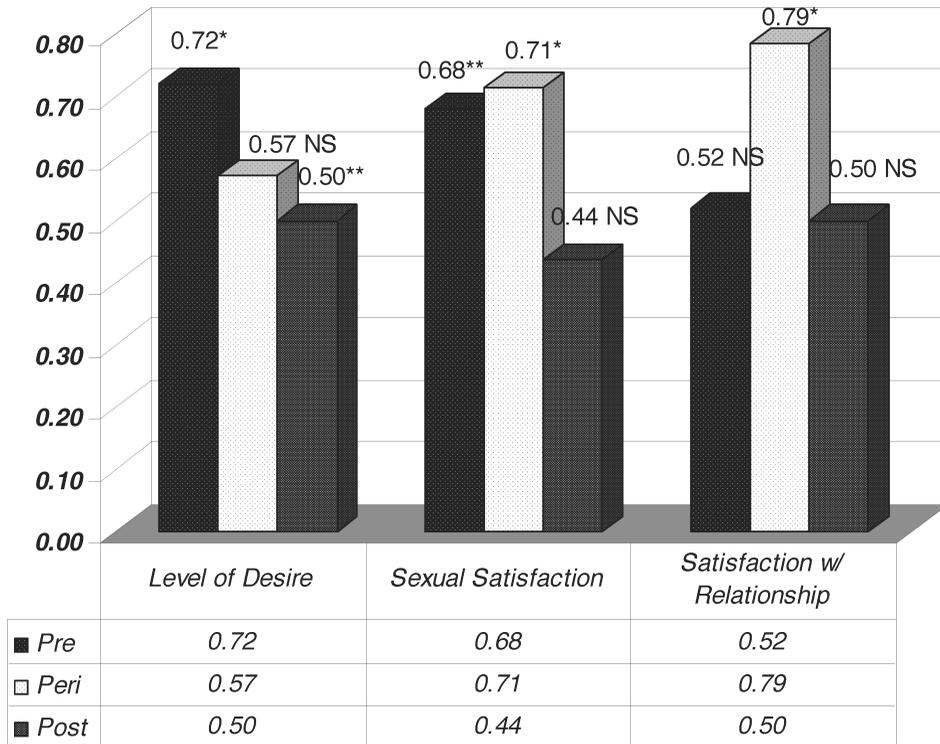
Question 5. Over the past 4 weeks how would you rate your level of sexual desire? (1 = Very low, 2 = Low, 3 = Moderate, 4 = High, 5 = Very high).

Question 6. Over the past 4 weeks how satisfied have you been with your overall sex life? (1 = Very dissatisfied, 3 = About equally satisfied and dissatisfied, 5 = Very satisfied).

Question 7. Over the past 4 weeks, how satisfied have you been with your sexual relationship with your partner? (1 = Very dissatisfied, 3 = About equally satisfied and dissatisfied, 5 = Very satisfied).

Question 8. Over the past 4 weeks, when you had sexual stimulation, how often did you have the feeling of orgasm? (1 = Almost never, 2 = A few times, 3 = Sometimes, 4 = Most times, 5 = Almost always).

Question 9. Over the past 4 weeks, when you had sexual stimulation or intercourse, how would you rate your degree of clitoral sensation? (1 = Very low, 2 = Low, 3 = Moderate, 4 = High, 5 = Very high).

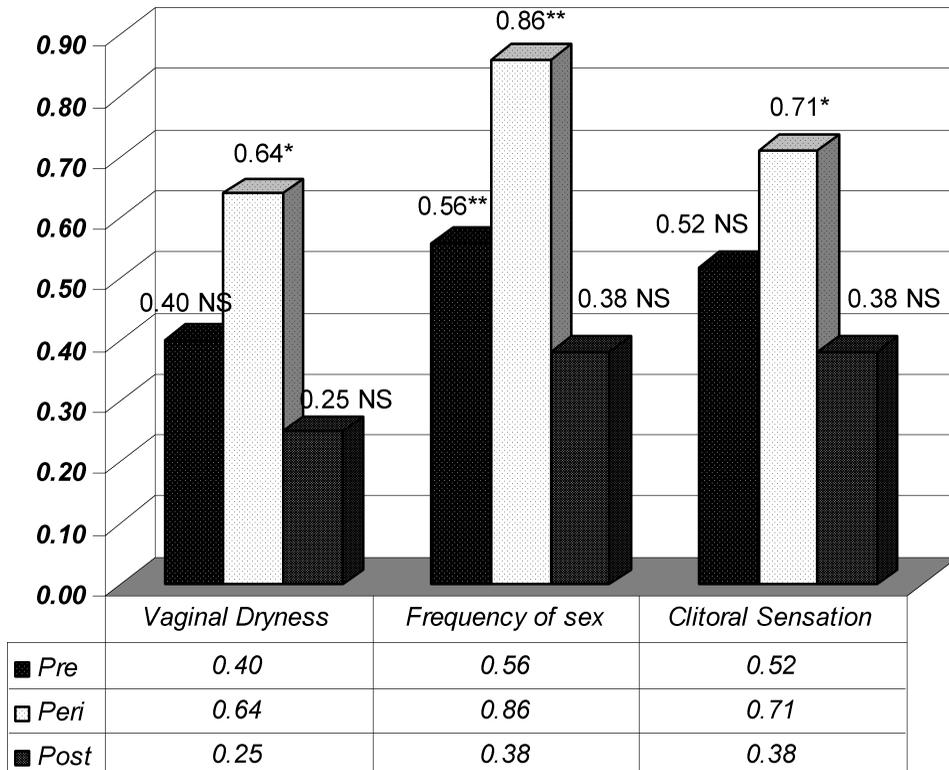


*, **, NS $p < 0.05$, $p < 0.01$ and not significant compared to placebo, respectively

FIGURE 1. Improvement of desire, satisfaction with sex life, and satisfaction with relationship among women on ArginMax compared with placebo.

Figure 1 demonstrates a shift away from desire as an important attribute in the PRE group toward satisfaction with sexual life and relationship in the PERI group, among those on ARG. The PERI group shows relatively more emphasis on satisfaction with sexual relationship compared with PRE group that emphasizes satisfaction with overall sex life. Figure 1 also shows the relatively smaller but still significant improvement seen in the POST group compared with PRE and PERI. These shifts were not seen in the placebo group.

Figure 2 demonstrates the greater effect in the PERI women on physical attributes such as vaginal dryness, frequency of sex, and clitoral sensation among those on ARG. These shifts were not seen in the placebo group. It is possible that this is the stage of life when these attributes are most at issue because of rapid changes or decreases in hormone-supported functions. However, the POST group shows much less improvement in these attributes than either of the other groups. At some point during late menopause, the decrease in ovarian hormones may become a more overwhelming factor.



*, **, NS $p < 0.05$, $p < 0.01$ and not significant compared to placebo, respectively

FIGURE 2. Improvement of vaginal dryness, frequency of sex, and clitoral sensation among women on ArginMax compared with placebo.

We noted no visual disturbance, blood pressure alterations, dizziness, hypersensitivity, or other significant side effects in any of the groups. Four participants in the treatment group noted minor gastric disturbances, two noticed heavier bleeding during menstruation, and one had increased incidence of headaches. Blood pressure measurements (systolic/diastolic) did not differ significantly in any group between initial and week-4 measurements (Table 4).

DISCUSSION

Despite the prevalence of sexual disorders among women, no efficacious pharmaceutical therapies are currently available. For example, administration of sildenafil in postmenopausal women did not significantly improve any attributes of sexual function, although there was some increase in vaginal

TABLE 4. Mean blood pressure measurements (systolic/diastolic) none of the values are significantly different between treatment groups ($p > 0.05$) student's *t*-test

Group	ArginMax		Placebo	
	Initial	4 Weeks	Mean	4 Weeks
All	118/74	121/73	119/74	120/74
Pre	116/72	119/73	115/72	116/74
Peri	117/75	123/74	117/76	120/73
Post	123/77	122/73	131/76	129/74

*None of the values are significantly different between treatment groups or between initial and week 4 ($p > 0.05$) Student's *t*-test.

lubrication and clitoral sensitivity (Kaplan et al., 1999). Clitoral discomfort and "hypersensitivity" occurred in 7 of 33 women (21%) in that study, 3 of whom withdrew from the study. Because nutritional approaches are generally milder and more multifaceted than pharmaceuticals, more exploration in this area may be warranted.

Although female sexual function is a complex result of psychological and physiological factors, nutritional supplementation appears to play a role in improvement of a number of key female sexual health parameters. The proposed mechanism of enhancement of the nitric oxide (NO) pathway with L-arginine only partially explains these results. NO derived from L-arginine is central to smooth muscle relaxation, vascular dilatation, and the regulations of circulation. The herbs and other nutrients in ArginMax may influence improvements in desire and sexual satisfaction not seen with sildenafil, except in certain arousal disorders (Basson et al., 2002).

In this study population, although limited in sample size, the PERI treatment group experienced increases in lubrication, clitoral sensitivity, satisfaction with relationship, and an accompanying increase in frequency of sexual intercourse, with higher significance than among the other menopausal groups. The PRE and POST menopausal groups also demonstrated increases in many attributes, but the differences in attributes among groups show a shift in emphasis from satisfaction with overall sex life in the PRE group to satisfaction with overall relationship in the PERI and POST groups. Also the PERI group shows less improvement in desire and more improvement in physical attributes such as improved vaginal lubrication, clitoral sensation, and frequency of sex, than the other groups. These differences may provide insight into the nature of changes that occur with changing reproductive function as women go through the menopausal transition and highlight specific issues that need to be addressed.

The decreased efficacy in the POST women may be due to the effect of androgens on the up-regulation of NOS. Even though many of the POST women were on HT, the declining androgens in the POST

group would down-regulate NOS (Munarriz et al., 2002; Traish, Kim, Min, Munarriz, & Goldstein, 2002; Berman et al. 2003). Combinations of nutritional and androgen therapy may show some promise for POST women. Because ArginMax has been shown to have no estrogen activity (Polan, Hochburg, Trant, & Wun, 2004), it may be a desirable alternative or adjunct to HT for sexual concerns. The increase in level of sexual desire (percent improved) seen across the entire ARG group may not be mediated by NOS.

Management of sexual health is an infrequently discussed yet extremely important subject for women. As consumers develop an ever-increasing interest in wellness-oriented approaches toward healthcare, the role of herbal and nutritional supplementation in sexual function may become more important. For women, in particular, research into potentially useful treatment therapies, preparations, or combinations is very much needed. Further investigation of differences in reactions among Pre, Peri, and Postmenopausal women may help shed light on the mechanisms involved.

CONCLUSIONS

Nutritional intervention has a positive effect on many attributes of sexual desire and satisfaction, but the type of attributes that improve shifted slightly among Pre, Peri, and Postmenopausal women in this study. PRE women displayed improvement primarily in desire and satisfaction with overall sex life, whereas PERI women showed improvement in satisfaction with sexual relationship and in physical attributes such as vaginal dryness, frequency of sex, and degree of clitoral sensation. POST women showed a slight but significant increase in desire.

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