



BRIEF COMMUNICATION

Red clover extract (MF11RCE) supplementation and postmenopausal vaginal and sexual health

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Approximately 75% to 85% of postmenopausal women seek medical attention due to symptoms of vaginal atrophy and atrophic vaginitis [1]. In Ecuador, 72.7% of postmenopausal women have been found to present vaginal dryness associated to decreased libido (76.5%) and sexual avoidance (75.2%) [2]. Although several options have been advocated for the treatment of postmenopausal vaginal atrophy, estrogens applied local or systemically continue to be an important one. Despite this, the recently reported results of the Women's Health Initiative (WHI) study have changed physicians' and patients' attitude towards hormone therapy, increasing their interest for alternative therapies.

Phytoestrogens and its main isoflavones (soy or red clover derived) are among these alternatives.

A prospective randomized, double-blind, placebo-controlled trial was carried out to evaluate the effect of a red clover extract (MF11RCE) supplementation over vaginal and sexual health of sixty postmenopausal women (amenorrhea >12 months and a basal FSH >30 mIU/mL), >40 years, non-hormone therapy users, with a basal Kupperman index ≥ 15 . After written consent, subjects were randomly assigned to one of two groups: either 2 capsules of MF11RCE (80 mg red clover isoflavones) per day for a 90 day period, or placebo of equal design. After a 7 day washout period, medication was crossed-over for another 90 days. Body mass index and vaginal/sexual health related indicators (dyspareunia, vaginal dryness and decreased libido, graded 0 to 3) were assessed at baseline, 90 and 180 days. At equal intervals vaginal cytologic sampling was performed for the determination of the karyopyknotic, cornification and basal cell maturation index. Placebo and MF11RCE capsules were placed in opaque containers (60 capsules each) labeled as A or B. Each capsule of MF11RCE (Menoflavon®) supplement provided approximately 40 mg isoflavones. Placebo and MF11RCE were provided by Melbrosin International, Produktions und Vertriebs GmbH & Co KG, Vienna Austria.

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Table 1 Effect on vaginal cytology after MF11RCE and placebo

| | Baseline (n=53) | After MF11RCE | After Placebo |
|--------------------------|-----------------|---|---|
| Karyopyknotic index (%) | 6.1 ± 11.7 | 45.6 ± 27.4 | 3.6 ± 7.6 |
| Mean change ‡ | | (-39.5; 26.5; -46.8 ~ -32.2) ^{a,*} | (42; 28.2; 34.3 ~ 49.8) ^{b,*} |
| Cornification index (%) | 6.1 ± 11.6 | 45.7 ± 26 | 3.9 ± 8.8 |
| Mean change | | (-39.6; 25.3; -46.6 ~ -32.7) ^{a,*} | (41.3; 27.1; 34.3 ~ 49.3) ^{b,*} |
| Parabasal cells (%) | 68.4 ± 36.7 | 1.9 ± 12.7 | 65.2 ± 37.4 |
| Mean change | | (66.4; 37.7; 56 ~ 76.9) ^{a,*} | (-63.2; 37.8; -73.6 ~ -52.8) ^{b,*} |
| Intermediate cells (%) | 27.4 ± 32.5 | 39.6 ± 25.4 | 30.2 ± 31.9 |
| Mean change | | (-12.2; 38.7; -22.9 ~ -1.5) ^{a,*} | (9.4; 35.8; -0.5 ~ 19.3) ^{b,*} |
| Superficial cells (%) | 4.2 ± 7.8 | 57.9 ± 25.9 | 4.7 ± 9.8 |
| Mean change | | (-53.8; 24.7; -60.6 ~ -47) ^{a,*} | (53.2; 28.5; 45.4 ~ 61) ^{b,*} |
| Vaginal dryness | 47 (88.7%) | 25 (47.2%) ^{a,*} | 44 (83%) ^{b,*} |
| Moderate-severe score | 33 (62.3%) | 4 (7.5%) ^{a,*} | 20 (37.7%) ^{b,*} |
| Dyspareunia ¹ | 41/52 (78.8%) | 18/52 (34.6%) ^{a,*} | 36/52 (69.2%) ^{b,*} |
| Moderate-severe score | 22/52 (42.3%) | 5/52 (9.6%) ^{a,*} | 15/52 (28.9%) ^{b,*} |
| Decrease of libido | 50 (94.3%) | 28 (52.8%) ^{a,*} | 39 (73.6%) ^{a, b,*} |
| Moderate-severe score | 38 (71.7%) | 13 (24.5%) ^{a,*} | 20 (37.7%) |

* Mean change or percentage was significantly different: ^a vs. baseline, ^b vs. red clover phase, $p < 0.05$; ‡ Values in parenthesis are: mean difference; standard deviation; 95% confidence interval; ¹ One subject was not considered for calculation as she was not sexually active.

Statistical analysis was performed with EPI-INFO 2000 statistical software (Centers for Disease Control, Atlanta, Ga., USA). Comparison of continuous and categorical data was performed with paired *t* student test and chi-square respectively. A *p* value of < 0.05 was considered as significant.

A total of fifty-three postmenopausal women completed the clinical trial. MF11RCE supplementation exerted a positive effect over the vagina which was evidenced by a significant improvement of the karyopyknotic, cornification and basal cell maturation index. This was correlated with a decrease in the rate of women having dyspareunia, vaginal dryness and decreased libido. Additionally the percentage of subjects presenting moderate to severe scorings within the latter mentioned parameters also decreased significantly (Table 1 and Fig. 1).

Studies demonstrating the positive effects of isoflavones over vaginal epithelium are scarce and

have been performed basically using soy bean compounds [3,4]. In the present study, compared to placebo, red clover (MF11RCE) supplementation had a significant beneficial effect over vaginal and sexual health in postmenopausal women supporting its use as an alternative option for the treatment of postmenopausal vaginal atrophy, especially in elder women with increased risk for cardiovascular events and/or breast cancer.

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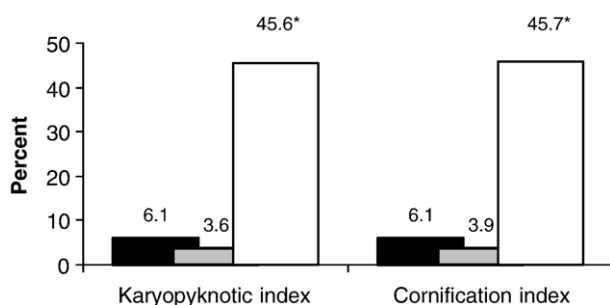


Figure 1 Karyopyknotic and cornification index at baseline (black bars), after placebo (gray bars) and after MF11RCE supplementation (white bars). Data given are means. *Mean value was significantly different compared to baseline and placebo ($p < 0.05$).