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PACR (Pine Bark Extract, L Arginine, L Citrulline, Rose Hip Extract) Improves Emotional, Physical Health and Sexual Function in Peri-Menopausal Women

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Abstract

Objective: Objective of the study was to evaluate the effect of PACR on sexual function and climacteric symptoms in peri-menopausal women. In addition, data of clinical chemistry and antioxidative capacity were collected.

Study design: In the double-blind, placebo-controlled study, 80 peri-menopausal women were supplemented with 4 tablets Lady Prelox® (PACR: Pine Bark Extract, L-Arginine, L-Citrulline, Rose Hip Extract) the day. Sexual function was evaluated by the Female Sexual Function Index (FSFI). Climacteric symptoms were ascertained by Women's Health Questionnaire and questions from the Kupperman's Index. Antioxidative activity and clinical chemistry was measured in blood samples of the participants by FSFI.

Results and conclusion: PACR improved sexual function as measured by 60% after 1 month and by 73% after 2 months treatment with PACR compared to baseline, increase of FSFI in the placebo group was only 40 and 46%. PACR relieved also climacteric symptoms evaluated by the Kupperman's index and Women's Health Questionnaire (WHQ). The efficacy of PACR was significantly superior compared to placebo. PACR also influenced metabolic parameters and antioxidant capacity of blood positively. No unwanted effects were reported. PACR improves sexual function and relieves climacteric symptoms in peri-menopausal women.

Keywords: Peri-menopause; Lady Prelox®; PACR (Pine Bark Extract; L-Arginine, L-Citrulline; Rose Hip Extract; Sexual function; Climacteric symptoms; Female Sexual Function Index.

Introduction

Menopause is defined by the permanent cessation of menstruation for 12 months secondary to a loss of ovarian activity. The post menopause is characterized endocrinologically by tonically elevated gonadotropin (Follicle Stimulating Hormone (FSH), Luteinizing Hormone (LH)) secretion, persistently low levels of ovarian steroids (estradiol, progesterone) and relatively low (50% decrease compared to younger age groups) testosterone secretion [1].

The menopause transition and the perimenopause are the transitional periods from reproductive to non-reproductive life actually taking place, when ovarian hormone production is declining and function, causing a host of symptoms [2].

The menopausal transition is characterised by fluctuating oestrogen levels, irregular menstrual cycles, and often a random mixture of oestrogen excess and oestrogen deficiency symptoms. These hormonal changes have substantial impact on the woman's sexual interest and capacity to become aroused and/or achieve orgasm.

The most common sexual difficulties reported by women across the perimenopause include dyspareunia, diminished desire, reduced arousal capacity and difficulty in achieving orgasm [3].

Lady Prelox®, a registered trademark of Horphag Research, has been developed to improve women's sex life and sexual function. This proprietary formulation consists of Pycnogenol® (French Maritime Pine Bark Extract), the amino acids L-Arginine and L-Citrulline, and a proprietary rose hip extract and is designated PACR. An exploratory investigational study on this proprietary formulation indicated a specific activity of Lady Prelox® for improving vascular and sensory aspects of healthy postmenopausal women [4]. The results clearly showed that Lady Prelox® administration for 2 months improved the Female Sexual Function Index.

The Female Sexual Function Index (FSFI) has been established and validated and nowadays represents the standard tool for assessment of women's sexual function [5].

The aim of this randomized, double-blind, placebo-controlled study was toevaluate the efficacy of PACR administered for improving/controlling mild to moderate sexualdysfunction in generally healthy women undergoing the menopause transition by the standardized questionnaire: The Female Sexual Function Index (FSFI) [5].

As Pycnogenol, the main constituent of PACR has been shown to improve menopausal symptoms, participants of the study answered related questions in the questionnaires of the Kuppermann Index and Hunters Woman Health Questionnaire (WHQ) [6-10].

The influence of PACR on basic parameters of clinical chemistry and antioxidative capacity should be evaluated in comparison to placebo.

Methods

Study population

Healthy, peri-menopausal, Bulgarian women, visiting the

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Department of Obstetrics and Gynecology of the Medical University of Sofia, with moderate sexual function problems (FSFI score < 26.55). They were 40-50 years of age, sexually active and fulfilled the inclusion and exclusion criteria. They were living in stable socio-economic circumstances.

Peri-menopausal women were characterized by menstrual cycles having disappeared for 2-11 months and appearing again. The hormonal status was defined by FSH > 30 IU/ml and E2 < 20 pg/L and endometrial thickness (vaginal sonography less than 6mm) with moderate discomfort of climacteric syndrome (Kupperman's index from 20 to 34).

Subjects needed to be in a stable monogamous relationship for more than 6 months.

All participants had a normal mammography and normal cervical smear (Pap-test).

Exclusion criteria

Were any systemic or acute disease, hormone replacement therapy, contraceptive medication, oophorectomy, hysterectomy, cardiovascular disease, renal and liver disease, hypertension, diabetes mellitus (fasting glucose ≥ 8mmol/l), endocrine abnormality, psychiatric disorders, ovarian disorders, concomitant treatment of sexual dysfunction.

Ethics

This study was approved by Ethics Committee of the Hospital "Maichindom", Sofia. Women gave written informed consent to participate in the study. Subjects could withdraw from the study for any reason at any time.

Randomization

Subjects were randomized by a computer generated random number list to receive either PACR or placebo in a double-blind fashion.

Medication

PACR and placebo identical in shape and appearance were packed with the same label. Neither participants nor investigators were able to identify verum or placebo.

Daily dosage was four tablets of PACR or placebo, two tablets taken in the morning and two tablets in the evening, for a period of eight weeks.

No other nutritional elements, vitamins or drugs were used in the observation period.

Study

Participants visited clinic for screening, enrollment and were followed after 1 and 2 months of treatment. At each visit, BMI, blood pressure, pulse, fasting glucose, lipid profile, hormone levels and TAC were assessed.

At the first visit (01.10-30.11.2009), the subjects underwent physical examination and medical history was recorded. Following data were collected: Age, marital status, time with current sexual partner, smoking, drugs / narcotic abuse, BMI, blood pressure, pulse, mammography, vaginal sonography and Pap test.

Blood samples were taken for clinical analysis with standard methods:

Haematology: Hemoglobin, leukocytes, erythrocytes, hematocrit, thrombocytes.

Fasting glucose, fasting cholesterol, HDL, LDL, triglycerides, SGOT/ASAT, SGPT/ALAT, Gamma-GT.

Hormones: LH, FSH, Prolactin, Estradiol, Progesterone, Testosterone.

Total antioxidant capacity

Total antioxidant capacity (TAC) of fresh plasma was assayed with ABTs cation radical decolorization [11]. The assay relies on the ability of antioxidants in the sample to inhibit the oxidation of ABTS® (2,2'-azino-di-[3-ethylbenzthiazoline sulphonate]) to ABTS® · + by methmyoglobin. The antioxidant capacity quantified as mmol Trolox equivalents.

Compliance and adverse effects

Participants were instructed on enrolment to report any unwanted effects. During the first month of treatment, participants were contacted by phone twice weekly by researchers to ensure compliance, to answer questions, provide instructions about tablet intake and questionnaires filling. The participants were asked for adverse effects and symptoms as per questionnaires. During the second month participants were contacted by phone once weekly.

Questionnaires

At each visit, baseline, 1 month and 2 months the sexual function of the study participants was evaluated by questionnaires translated to Bulgarian, as the FSFI,theKupperman Menopausal Index and the Women's Health Questionnaire of Hunter (WHQ).

Female sexual function index (FSFI)

The Female Sexual Function Index (FSFI) is a multidimensional self-reporting questionnaire that has the advantage over other instruments – such as diaries or calendars – that it allows a quantitative evaluation of sexuality changes after therapeutic interventions [5].

This instrument is composed of 19 questions, grouped in six domains; desire (items 1 and 2); arousal (items 3-6); lubrication (items7-10), orgasm (items 11-13), satisfaction (items 14-16) and pain (items 17-19). Each question has 5 or 6 options, assigning a score ranging from 0 to 5. The value of each domain is multiplied by a factor determined by Rosen et al., the final result is the arithmetic sum of the different domains [5]. The higher the FSFI score, the better the sexuality of women. Subjects with a total FSFI score of < 26.55 were defined according to Rosendal as having sexual dysfunction.

Kupperman index

Kupperman's index assesses the level of discomfort of climacteric syndrome (General assessment): Hot flashes, night sweats, sleep problems, irritability, depressed mood, memory (concentration), vertigo (dizziness), headache, backache / pain limbs, palpitation [9].

The Kupperman's index lists 10 symptoms classified as menopausal in order of their importance. Each one of the symptoms were given a certain weight (conversion index) which when multiplied by the score observed gave us the corrected score of the symptoms. Thus the symptom "hot flashes" was given aweighting (conversion index) factor of 4, whereas the symptom "night sweats", "sleep problem" and "irritability" are given a weighting factor of 2. The other symptoms, namely "depressed mood", "memory (concentration)","vertigo

(dizziness)","headache", "backache/pain limbs" and "palpitation" are given a weight of only 1. For each symptom the Kupperman's index recognizes 4 grades of severity according to the following criteria: 0 = none; 1 =mild; 2 = moderate; and 3 = severe. The complaints were rated by physician but not by participants.

In the practice the Kupperman's index makes it possible to quantify the symptomatic severity of the menopausal syndrome, considering no (zero) symptoms: no complaints, mild (< 15), moderate (15-20) and severe (> 20).

Hunter's WHQ

The WHQ is a 36 item scale developed to measure emotional and physical symptoms in middle-aged women and it contains nine subscales. The WHQ was translated into Bulgarian. The WHQ subscales include: depressed mood (7 items), anxiety/fears (4 items), sleep problems (3 items), somatic symptoms (7 items), menstrual symptoms (4 items), vasomotor symptoms (2 items), memory/concentration (3 items), attractiveness (2 items), and sexualbehavior (3 items). The attractiveness subscale includes questions about self-esteem. Symptom severity was scored as follows: 4 = no discomfort, 3 = little discomfort, 2 = clear discomfort, 1 = heavy discomfort; thus the higher the score, the less severe the symptom distress and dysfunction.

The highest score means the least pronounced the distress and dysfunction [10].

Analysis of data

Data were analyzed using SPSS software (v 17.0.1; SPSS Inc, Chicago, IL). Descriptive statistics were applied (mean, standard deviation, and amplitude) to characterize the age, body mass index, systolic and diastolic blood pressure using Student's t-test for two independent samples.

Repeated measures ANOVAs were applied to detect significant differences between groups in evaluation of results of FSFI domain scores, Kupperman's index and WHQ symptoms. The level of statistical significance was established at $P < 0.05$.

Results

Study population

A total of 80 Bulgarian women aged 40 to 50 years were enrolled in the present study. The women were patients of the Department of Obstetrics and Gynecology of the Medical University Sofia. The subjects were randomly allocated to PACR (n=40) or to placebo (n=40). All 80 participants enrolled, completed the 2-month treatment period. All participants were employed andnon-smokers.

None of the participants terminated the study because of unwanted effects of treatment.

The mean age of all participants was 45.41 ± 2.37 years (range 40-50). The two treatment groups were comparable for age, height and weight.

The two groups differed slightly as women in the PACR grouppresented with a significantly lower BMI and higher values of systolic and diastolic blood pressure (SBP and DBP) than women in the placebo group. The differences in the values were not clinically relevant andboth groups were considered homogeneous.

Effect of treatment on the women's sexual function

The Female Sexual Function Index (FSFI) was used to assess sexual function in women.

FSFI domain scores and full scale scores for PACR and placebo are presented in Table 1.

At baseline, the FSFI domain scores and the total scores were significantly higher in the PACR group, showing a better sexual function compared to subjects in the placebo group. During the treatment period, all FSFI domain scores and full scale scores increased to a significantly higher degree in the treatment arm compared to the placebo. The totalFSFI score improved by 60% after one month and by 73% after two month treatment with PACR compared to baseline, whereas the increase was limited to 40 and 46% respectively in the placebo group.

As previously stated, a score of 26.5 has been suggested by Rosendal as delineating 'functional' from 'dysfunctional' sexual function in women. After 2 months treatment the FSFI score reached the limit with 26.49 in the PACR group. The improvement is clinically significant.

Effect of treatment on climacteric symptoms

Kupperman's index (KI): At baseline the PACR group presented slightly higher global KI score. In particular, vertigo, headache, joint pain and palpitation scored statistically higher in the treatment group compared to placebo at baseline (Table 2). However, the most frequent complaints for women in both groups as hot flashes, night sweats, sleep problems and irritability were equally scored.

At the first month most parameters of the Kupperman's index were lower in the PACR group showing a relief of the menopausal symptoms by the supplementation. Hot flashes, night sweats, sleep problems and irritability were markedly reduced in women taking PACR, but not influenced by placebo. Only the parameter palpitation was more lowered in the placebo group. Vertigo was equally scored.

	Baseline		1 month visit		2 month visit	
Parameter	**PACR**	**Placebo**	**PACR**	**Placebo**	**PACR**	**Placebo**
	$\overline{X}$ **(SD)**	$\overline{X}$ **(SD)**	$\overline{X}$ **(SD) %**	$\overline{X}$ **(SD) %**	$\overline{X}$ **(SD) %**	$\overline{X}$ **(SD) %**
Desire	2,58 (0,43)	2,13 (0,51)	3,50 (0,54) 58	2,13 (0,51) 36	4,23 (0,66) 71	2,67 (0,51) 45
Arousal	2,85 (0,59)	2,13 (0,51)	3,72 (0,53) 62	2,40 (0,00) 40	4,47 (0,62) 75	2,67 (0,51) 45
Lubrication	2,85 (0,59)	2,13 (0,51)	3,72 (0,53) 62	2,40 (0,00) 40	4,53 (0,62) 76	2,76 (0,56) 46
Orgasm	2,85 (0,59)	2,13 (0,51)	3,69 (0,57) 62	2,40 (0,00) 40	4,46 (0,64) 74	2,73 (0,54) 46
Satisfaction	2,85 (0,59)	2,13 (0,51)	3,63 (0,64) 61	2,40 (0,00) 40	4,47 (0,61) 75	2,73 (0,54) 46
Pain	2,52 (0,53)	1,77 (0,61)	3,39 (0,54) 57	2,67 (0,51) 45	4,32 (0,65) 72	3,06 (0,60) 51
Total FSFI	16,50 (2,85)	12,42 (2,25)	21,65 (2,79) 60	14,40 (0,82) 40	26,49 (3,28) 74	16,62 (2,30) 46

Differences of parameters for PACR and placebo are highly significant ($p< 0.001$) for each parameter.

Table 1: FSFI domain scores and full scale scores visit for PACR and placebo.

	Baseline		1 month visit		2 month visit	
Parameter	**PACR**	**Placebo**	**PACR**	**Placebo**	**PACR**	**Placebo**
	$\overline{X}$ **SD**	$\overline{X}$ **SD**	$\overline{X}$ **SD**	$\overline{X}$ **SD**	$\overline{X}$ **SD**	$\overline{X}$ **SD**
Hot flashes	7,90 (0,63)	8,00 (0,00)	4,30#* (1,97)	8,00 (0,00)	4,00#* (0,00)	8,00 (0,00)
Night sweats	3,95 (0,32)	4,00 (0,00)	2,15#* (0,53)	4,00 (0,00)	2,00#* (0,00)	4,00 (0,00)
Sleep problems	3,95 (0,32)	4,00 (0,00)	2,15#* (0,53)	4,00 (0,00)	2,0#*0 (0,00)	4,00 (0,00)
Irritability	3,95 (0,32)	4,00 (0,00)	2,05#* (0,32)	3.95 (0,32)	2,00#* (0,00)	4,00 (0,00)
Depressed mood	1,93 (0,35)	1,98 (0,16)	1,10#* (0,30)	1,83* (0,38)	1,00#* (0,00)	1,68* (0,47)
Memory (concentration)	1,83 (0,50)	1,88 (0,33)	0,98#* (0,36)	1,73* (0,45)	0,95#* (0,22)	1,55* (0,60)
Vertigo (dizziness)	1,53 (0,60)	1,20# (0,56)	0,65* (0,53)	0,68* (0,73)	0,28* (0,45)	0,53* (0,72)
Headache	1,88 (0.33)	1,60# (0,50)	0,98#* (0,16)	1,45* (0,55)	0,93#* (0,27)	1,35* (0,53)
Backache / limb pain	1,83 (0,38)	1,55# (0,50)	0,98#* (0,16)	1,43* (0,50)	0,95#* (0,22)	1,20* (0,56)
Palpitation	1,65 (0,53)	1,15# (0,53)	0,78* (0,42)	0,73* (0,51)	0,65* (0,48)	0,30#* (0,46)
Total score	30, 38 (2,56)	29,35# (1,99)	16,10#* (1,92)	27,78* (2,22)	14,75#* (0,95)	26,60* (1,98)
Percentual change of total score of Kupperman's index to baseline:			46,6% (7,59)	5,42% (2,80)	51% (6,14)	9,34% (3,61)

The asterisk (*) indicates statistical significant changes compared to baseline, the number sign (#) indicates statistical significant difference between PACR and Placebo.

Table 2: Kupperman's index by visit (for each group).

The improvement of the total KI score relative to baseline was much higher in the PACR group in comparison to placebo. ThePACR group improved by 46,6% after one month and by 51,02% after 2 month treatment, whereas, the improvement in the placebo group was limited to 5,42% and 9,34%, respectively. The difference between the 2 groups is highly significant ($p< 0.001$).

Women's health questionnaire: Climacteric symptoms were additionally evaluated by the Women's Health Questionnaire (WHQ). The higher the score, the less pronounced is the suffering and dysfunction.

A comparative analysis of the presence of climacteric symptoms, assessed by the Women's Health Questionnaire (WHQ) was done independently for each group by visit (Table 3). During the baseline visit, women in the PACR group presented with significantly slightly higher scores of most WHQ symptoms, compared to women in the placebo group. Only one complaint was more prevalent among subjects in the placebo group as signs of somatic symptoms (tiredness, headaches, dizziness, backache, sickness, pins and needles in the hands or feet). During the treatment period (visit 2 and 3) all WHQ symptoms improved significantly better in the PACR group compared to placebo.

The most common complaint reported by participants from both groups was the presence of vasomotor symptoms.

The relative improvement of the WHQ symptoms expressed in percentage is significantly much better in the PACR group compared to placebo after 1 month and even more pronounced after 2 months treatment. It ranged from 33 to 46% after one month and from 53 to 81% after 2 months treatment in the PACR group while improvement in the placebo group ranged from 6 to 32% after one month and from 13 to 64% after 2 months. It is interesting to note that attractiveness is the symptom that was most improved by placebo (64%).

Blood pressure, fasting glucose BMI, lipid profile and antioxidant capacity: Most of the tested parameters for clinical chemistry remained unchanged, data not shown. Of interest is the influence of PACR on blood pressure. At baseline, systolic and diastolic BP were both higher in the PACR group (Table 4). After one month treatment, there was no difference in BP between both groups and after 2 month treatment the BP was lower in the PACR group, showing a clear effect of PACR on improving blood pressure.

Fasting glucose was similar in both groups at baseline,but decreased in the PACR group. After 2 months, fasting glucose decreased significantly from 4.8 - 4.4mmol/l. However, blood glucose remained within normal clinical values.

Fasting total cholesterol and triglycerides levels did not change significantly in both groups.

In contrast, the HDL significantly increased in the PACR group compared to placebo and the LDL cholesterol followed the inversed trend. Consequently, the LDL/HDL ratio improved, the change was statistically highly significant.

Body mass index (BMI) was higher at baseline in the placebo group 25.58 vs 24.96 and remained stable during the 2 month study. BMI in the PACR group decreased during the study period; however, the small changes were significant.

The total antioxidant capacity was comparable before the study start and remained constant in the placebo group. In the PACR group, it regularly increased from 1.24 to 1.36 and 1.48 µmol Trolox, showing the antioxidant power and bioavailability of PACR, while no change was seen in the placebo group. The increase was statistically highly significant.

Safety: No side-effects due to treatments were observed. No significant changes from baseline values were observed in vital signs and blood parameters measured at inclusion and after 6 months (end of treatment) like ALAT, ASAT, gamma-GT, Alkaline Phosphatase, CRP, Serum creatinine as well as for blood cell count and fibrinogen, aPTT, and PT (Quick's value) and hematocrit.

Discussion

Sexual functioning is an imperative component of women's lives and has progressively received public health, medical and even pharmaceutical attention [12]. More than 75% of the middle-aged women in the Study of Women's Health Across the Nation (SWAN) reported that sex was moderately to extremely important to them [13].

This study targeted women undergoing peri-menopause and presenting with moderate sexual dysfunction (as defined by FSFI score < 26.55). The results showed that supplementation with Lady Prelox® (PACR) improved the sexual function in accordance with a previous

Parameter	1 month visit			2 month visit		
	PACR	Placebo	placebo	PACR	Placebo	placebo
	$\overline{X}$ (%)	$\overline{X}$ (%)	p	$\overline{X}$ (%)	$\overline{X}$ (%)	$\overline{X}$ (%)
Depressed mood	33,14#	6,67	<0,001	63,78#	13,34	<0,001
Somatic symptoms	46,74#	7,00	<0,001	81,93#	14,39	<0,001
Memory/concentration	43,78#	23,71	<0,001	80,25#	47,93	<0,001
Vasomotor symptoms	38,21#	22,34	<0,001	53,92#	41,46	<0,001
Anxiety/fears	47,83#	17,30	<0,001	77,50#	34,60	<0,001
Sexual behaviour	37,05#	20,69	<0,001	70,94#	40,88	<0,001
Sleep problems	37,47#	20,69	<0,001	72,20#	41,03	<0,001
Menstrual symptoms	28,72#	14,02	<0,001	56,15#	28,04	<0,001
Attractiveness	39,13	32,92	0,038	61,00#	64,17	0,048

The asterisk (*) indicates statistical significant changes compared to baseline, the number sign (#) indicates statistical significant difference between PACR and Placebo.

Table 3: Mean improvement (in %) of WHQ symptoms relative to baseline in PACR group and placebo.

Parameter	Baseline		1 month visit		2 month visit	
	PACR	Placebo	PACR	Placebo	PACR	Placebo
	$\overline{X}$ SD	$\overline{X}$ SD	$\overline{X}$ SD	$\overline{X}$ SD	$\overline{X}$ SD	$\overline{X}$ SD
SBP (mmHg)	128,13# (3,87)	124,0 (3,95)	120,13 (2,40)	120,50 (2,48)	114,00 (3,24)	119,88# (1,79)
DPB (mmHg)	81,63# (3,28)	80,25 (1,10)	79,25 (1,81)	79,75 (1,58)	75,00 (1,60)	79,50# (1,52)
BMI (kg/m²)	24,96 (0,59)	25,58# (0,61)	24,54* (0,51)	25,35# (0,64)	24,18* (0,48)	25,26# (0,70)
Fasting Glucose (nmol/L)	4,80 (0,44)	4,84 (0,45)	4,61 (0,42)	4,73 (0,35)	4,45 (0,45)	4,79# (0,40)
HDL (nmol/L)	1,87 (0,18)	1,89 (0,17)	1,91# (0,09)	1,87 (0,10)	1,97# (0,19)	1,88 (0,13)
LDL (nmol/L)	1.94 (0,04)	1,93 (0,16)	1,88 (0,10)	1,93# (0,16)	1,86 (0,15)	1,96# (0,09)
LDL/HDL ration	1,04 (0,08)	1,03 (0,08)	0,99 (0,07)	1,03 (0,07)	0,96 (0,15)	1,04 (0,02)
Total antioxidant capacity (TAC) (µmol Trolox)	1,24 (0,05)	1,23 (0,03)	1,36# (0,05)	1,23 (0,03)	1,48# (0,07)	1,23 (0,04)

The asterisk (*) indicates statistical significant changes compared to baseline, the number sign (#) indicates statistical significant difference between PACR and Placebo.

Table 4: Blood pressure, fasting glucose, BMI, lipid profile and TAC for PACR and placebo by visit.

exploratory study with PACR in women in the post-menopausal status, showingan improvement of the sexual function [4].

Mechanism

The positive effect of PACR is based on the enhancement of the production of endothelial nitric oxide synthase (eNOS). Sexual arousal stimulates e-NOS within the female sexual organs to produce nitric oxide (NO) from the aminoacides L-arginine and L-citrulline. The NO dilates the blood vessels in the female sexual organs thus increasing selectively the circulation inside the target organ. PACR contains Pycnogenol which stimulates synthesis of e-NOS [14]. The greater amount of e-NOS together with a greater amount of precursors for NO, as L-arginine and L-citrulline enables the production of a large quantity of NO, so that the tissues of the other female organs are subject to increased circulation.

The effects of PACR on menopausal symptoms are in line with the effects of Pycnogenol, one of the constituents of PACR, on menopausal symptoms [6-8]. The studies showed that largely all climacteric symptoms improved to varying degrees, especially the vasomotor-related hot flashes. The exact physiologic mechanism responsible for the symptom improvement remains unclear. However, it is known that Pycnogenol® does not bear phyto-estrogen-like activities [15]. Furthermore, in clinical trials carried out with Pycnogenol® in women at child-bearing age, no effects on E2 estradiol values were detectable[16]. The absence of oestrogen-like activities of ingredients present in the PACR formulation represents an important aspect, as there is a great public sensitivity towards unwanted hormonal activities.

The higher antioxidative capacity of blood in the PACR group is most probably the result of the antioxidative effect of Pycnogenol, Rohdwald re-inforced by the antioxidative vitamins E and C in the rose hip extract [15].

The present study also confirms the positive impact of PACR on cardiovascular risk factors in women undergoing peri-menopause by decreasing blood pressure, blood glucose, total anti-oxidant capacity and by improving the lipid profile. This is particularly important as menopause is associated with an increased risk of cardiovascular diseases [17].

The effects of the constituent of PACR, Pycnogenol®, on blood glucose lowering have already been demonstrated in diabetic patients and in subjects with metabolic syndrome [18-21]. Therefore, the slight lowering of blood glucose by PACR can be deduced from the anti-diabetic effect of Pycnogenol. A small, but significant decrease of BMI had also been observed in a study with context to an improvement of the symptoms of the metabolic syndrome, Stuard et al. [21] and could be probably related to a generally better function of metabolic processes.

In conclusion, this study confirms the potential of Lady Prelox® (PACR) to improve sexual function in women undergoing peri-menopause. Beneficial effects on climacteric symptoms and the cardiovascular risk profile including the reduction of oxidative stress by an increase of antioxidative capacity could be demonstrated.

Contributors

R. Stanislavov performed all clinical tests. P. Rohdewald evaluated the results and wrote the publication.

Competing Interest

P. Rohdewald is consulting Horphag Research Ltd. R. Stanislavov received the grant from Horpahg Research Ltd to perform the clinical study.

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