Research Article

Effects of D-003 (Sugarcane Wax Acids) (10 mg/day) on the Quality of Life of Postmenopausal Women: A Randomized, Double-Blinded Study.

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ABSTRACT

Osteoporosis (OP), common disease characterized by low bone mineral density (BMD) and increased risk of fractures that affects primarily postmenopausal women, has been associated to impaired health-related quality of life (QoL) and significant morbidity and mortality. Inhibitors of osteoclastic bone resorption remain as first-line pharmacological treatment of OP. D-003, a mixture of high molecular weight sugarcane wax acids, ameliorated bone resorption and bone mass loss in experimental OP. D-003 (10 mg/day) given for 6 months reduced resorption markers, and given for 3 years increased lumbar BMD and improved QoL in postmenopausal women with low BMD. This study investigated the effects of shorter (3 months) treatment with D-003 on QoL of postmenopausal women with moderate to high OP risk. Forty women were randomized, under double-blind conditions, to placebo or D-003 (10 mg/day). The primary efficacy outcome was the significant reduction of the total score of Quality of Life European Foundation for Osteoporosis (QUALEFFO) questionnaire versus placebo. The significant reduction of serum low-density lipoprotein-cholesterol (LDL-C) was the secondary outcome. Safety indicators and adverse experiences (AE) were controlled. Baseline characteristics were similar in both groups. D-003 decreased significantly ($p<0.0001$ vs baseline, $p<0.05$ vs placebo) the total (29.2% versus baseline, 34.5% versus placebo) and pain, physical activity and health perception-QUALEFFO scores. Also, D-003 lowered significantly serum LDL-C (17.1%). Treatment was safe and well tolerated. No withdrawals due to AE. Only 4 placebo-treated subjects experienced AE. In conclusion, D-003 (10 mg/day) given for 3 months improved QoL in postmenopausal women with moderate to high OP risk, and reduced serum LDL-C.

Keywords: D-003, sugarcane wax acids, osteoporosis, antiresorptive therapy, postmenopausal women

INTRODUCTION

Osteoporosis (OP), a highly prevalent systemic skeletal disease, is characterized by low bone mass, impairment of bone quality, bone fragility, and increased risk of low impact fractures.[1-3]

OP affects primarily postmenopausal women (about 30%) worldwide.[3,4] OP has been associated to significant morbidity and mortality, mainly in the elderly.[3-5]

Postmenopausal OP affects millions of women, and numbers expected to double in 2050.[3] Pathogenesis of postmenopausal OP involves estrogen deficiency, a normal feature of women aging, as pivotal factor.[5,6]

Nowadays, women may live decades after menopause, but OP and other chronic illnesses will affect their lifespan and quality of life (QoL) from their sixties and beyond.[7]

OP is mostly asymptomatic until a subject suffers a fracture, which often leads to restriction of independence and increased risk of further falls. Consequently, OP impacts the QoL of sufferers.[5,6-9]

Adequate intake of Vitamin (Vit) D, bodyweight control and regular physical activity are the mainstay of non-pharmacological intervention, which provides pain reduction, prevention of falls, and improvement of mobility and QoL.[10,11] Consumption of calcium supplements remain controversial because of their unfavorable risk/benefit profile supported by small benefit on fractures and increased cardiovascular risk.[12]

Pharmacological intervention of OP results from the knowledge of bone remodelling, a process that maintains the integrity of the skeleton in adults throughout a balance between bone resorption and formation, regulated by osteoclasts and osteoblasts, respectively.

There is growing evidence that cholesterol synthesis and osteoclast activation share a common pathway from mevalonate. Moreover, increased lipid oxidation contributes to osteoporosis pathogenesis since products of lipid oxidation promote osteoblastic differentiation of vascular cells (boned arteries) and inhibit such differentiation in bone cells (brittle bones).[13,14]

Antiresorptive agents that inhibit osteoclastic bone resorption represent the cornerstone of pharmacotherapy of OP. Bisphosphonates (BP) are the first-line therapy for patients with OP at high fracture risk, but their long-term intake has been linked with some serious adverse events (AE).[6,15]

BP inhibit bone resorption by increasing osteoclast apoptosis through the inhibition of geranylgeranyl diphosphate formation, the substrate for the prenylation of most GTP binding proteins involved in the mevalonate to cholesterol pathway. GTP protein prenylation is required for osteoclast activation, so that its inhibition

prevents isoprenoid production and then osteoclast formation and activity, and increases osteoclast apoptosis.[16]

Teriparatide, the only anabolic drug approved, is used in severe OP only due to safety matters and high cost. Hormone replacement therapy (HRT) may preserve/increase BMD in postmenopausal women, but their AE profile, including increased risk of thromboembolic events and breast cancer, has limited its use to climacteric symptoms. Selective estrogen modulators (SERMs) maintain or increase vertebral and femoral BMD and may lower fracture risk.[3,4,6] Phytoestrogens use is still in debate, so that they are not recommended for postmenopausal OP.[17]

D-003, a mixture of higher aliphatic acids isolated from sugar cane wax wherein octacosanoic acid is the most abundant, has been shown to inhibit cholesterol synthesis prior to mevalonate formation by regulating HMGCoA reductase activity.[18,19] Also, D-003 has been effective for inhibiting lipid peroxidation.[20-24] Effects of D-003 derived from these two actions were then expected.

Consequently, D-003 ameliorated ovariectomy-induced bone loss and bone resorption in rats by increasing osteoclasts apoptosis,[25-29] and attenuated bone loss and osteonecrosis in prednisolone-induced OP in rats.[30] D-003 is devoid of estrogenic action.[31] D-003 (10 mg/day) given for 6 months reduced the urinary excretion of deoxypyridinolin (DPD)/creatinine, a bone resorption marker,[32] and administered for long-term (3 years) increased significantly lumbar spine BMD, improved QoL and reduced bone/joint/muscle complaints as compared to placebo in postmenopausal women with low BMD.[33]

Changes on biochemical surrogates of OP and BMD require at least 6 months and years, respectively,[34] while OP-related QoL may improve as soon as 3 months after starting some interventions.[35] Different approaches may be used to assess health-related QoL, but the questionnaire of the European Foundation for Osteoporosis (QUALEFFO) is that commonest used.[36] Versions of QUALEFFO have been translated and validated, so that this tool is very useful to assess the extent of QoL impairment and the efficacy of interventions.[37-41]

In light of these issues, this study investigated the short-term effects of D-003 (10 mg/day) on the QoL of postmenopausal women with moderate to high OP risk.

PARTICIPANTS AND METHODS

Study Design

The study protocol was approved by the Institutional Ethical and Scientific Review Board.

Postmenopausal women with prior diagnosis of osteopenia (T-score measured by dual-energy X-ray absorptiometry ≤−1.0)[42] were recruited from the Orthopaedic Unit of the Surgical Medical Research Centre (Havana, Cuba) after proving their informed written consent (Visit 1). All participants underwent physical examination, blood sampling and medical history, and were interviewed about their osteoporotic risk factors.[42]

No special diet was followed in the study, except for those women with high serum total cholesterol values (≥5.0 mmol/L) who were encouraged to continue or start on a low-fat, low-cholesterol diet during the trial.

Eligible women were randomized (Visit 2), under double-blind conditions, to placebo or D-003 (10 mg/day) for 3 months. They attended to follow-up visits at 1, 2 and 3 months on treatment (Visits 3 – 5). Physical examination and quality of life questionnaire (QUALEFFO 41)[36,37] were performed at each visit. Treatment compliance and adverse experiences (AE) were controlled from visits 3 to 5. Laboratory analyses were performed at baseline and after 3 months on treatment.

Participants

To be enrolled, women (40 – 70 years) should have had amenorrhea for at least 12 months prior to the recruitment, a diagnosis of osteopenia and some of the following OP risk factors: personal or family history of fractures, low dietary calcium intake, physical inactivity, cigarette smoking, small, thin frame; Caucasian or Asian race, excess of alcohol drinking, and consumption of corticoids and/or thyroid medications.

Enrolled women were eligible for randomization if their OP risk factor value was ≥ 10 (moderate to high) according to a score for OP risk evaluation.[43] Exclusion criteria included: diastolic blood pressure above 90 mm Hg, renal or liver dysfunction, diagnosed neoplasia, uncontrolled diabetes, and thyroid-related diseases and clinically significant vitamin D deficiency. Women who were taken any drug affecting bone metabolism (antiresorptive drugs, glucocorticoids, thyroid hormones) and those with serious AE occurred in the 6 months prior to the trial were also excluded.

Treatment

Participants were randomized, in a double blind fashion, to take D-003 (10 mg/day) or placebo tablets with the evening meal for 12 weeks. The dose selected was that used in previous studies in postmenopausal women.[31,32]

Treatment was assigned by a computer-generated code. Women were randomized in blocks of 10 and a randomisation ratio 1:1. Each package of study medication was labelled with an allocation code that should be revealed only in case that a serious AE happened to a study subject. Participants and all study staff, except those who generated the allocation code, remained blinded to treatment allocation during the whole trial.

Treatment compliance was assessed at each visit through patient reports and tablet counts. Compliance was considered good and very good if the participants had

consumed at least 85% and 90%, respectively, of the scheduled doses from the previous visit.

Consumption of any drug affecting bone metabolism (antiresorptive drugs, glucocorticoids, thyroid hormones) or of drugs inhibiting cholesterol synthesis was prohibited from enrolment up to study completion.

Study Outcomes

The primary evaluation criterion was the effect of treatment on the QoL evaluated by QUALEFFO-41 questionnaire. This questionnaire, developed for measuring quality of life in patients with vertebral deformities, comprises 41 questions structured in five domains: pain, physical function, social function, general health perception, and mental function. This tool has been validated and translated to different languages, including the Spanish one.[37-41]

Taking into account the cholesterol-lowering effects of D-003[18,19,23,24] and that hypercholesterolemia is a frequent coronary risk factor among postmenopausal women we selected the significant reduction of serum low-density lipoprotein-cholesterol (LDL-C) as secondary efficacy outcome.

Safety and Tolerability

Safety and tolerability analyses included data on AE and safety indicators.

AE were defined as occurrence of any untoward condition, including minor illnesses, during the study, regardless of whether they were or not treatment-related.

All information on AE was gathered at each participant contact. Since potential fractures were not efficacy outcomes they were included in the AE analysis, and should be identified by self-report and confirmed by radiology or surgical reports.

According to their intensity, AE were classified as mild, moderate or serious. Mild AE did not require stopping of study products or specific treatment; moderate AE were those requiring withdrawal of study products and/or treatment of AE.

Serious were those fatal (leading to death) or life threatening (leading to or prolonging hospitalizations).

Safety indicators included physical (bodyweight, heart rate, arterial pressure) and blood biochemistry (alanine–ALT- and aspartate aminotransferase–AST-, glucose and creatinine) variables.

Laboratory Determinations

Blood samples were collected after 8-10 hours overnight fast. Serum total cholesterol (TC) and triglycerides (TG) were determined through enzymatic methods with reagent kits from Roche (Basel, Switzerland), whereas high-density lipoprotein-cholesterol **(**HDL-C) was determined as the cholesterol content in the supernatant obtained after ß-lipoproteins precipitation.[44] Low-density lipoprotein-cholesterol **(**LDL-C) values were calculated with the Friedewald equation.[45]

Blood biochemistry safety indicators were determined with enzymatic methods using reagent kits from the same supplier. Analyses were done in a Hitachi 719 autoanalyzer (Tokyo, Japan) at the Medical Surgical Research Centre (Havana, Cuba).

A systematic quality control was performed throughout the study, which controlled the precision (within and between-day variations) and the accuracy (comparisons against reference standards) of the methods.

Statistical Analysis

A sample size of 40 women/treatment group was expected to provide 80% power to detect a 25.0% between-group difference in the mean percent change from baseline in QoL questionnaire. Data analyses were according to intention to treat (ITT), including all randomized subjects, as randomized, regardless of study medication adherence.

Continuous variables were analysed with the Wilcoxon test for matched samples (within group comparisons), and with the Mann Whitney u test (between group comparisons). Results were confirmed by ANOVA. Categorical variables were compared with the Fisher's Exact Probability Test. All statistical analyses were performed using Statistics data analysis software, from Windows.

RESULTS

Baseline Characteristics and Withdrawals

Table 1: Baseline characteristics of Study Population

	D-003 (n=20)		Placebo (n=20)		Total (n=40)	
Age (X ± SD)	56 ± 7		56 ± 9		56 ± 8	
Osteoporosis risk	12.0 ± 1.3		12.7 ± 1.2		12.4 ± 1.3	
Body mass index (X ± SD)	27.2 ± 4.4		27.2 ± 4.5		27.2 ± 4.4	
Personal history	**n**	**%**	**n**	**%**	**n**	**%**
Low dietary calcium intake	18	90.0	20	100.0	36	90.0
Prior fractures	15	75.0	19	95.0	34	85.0
Family fractures	15	75.0	13	65.0	28	70.0
Hypercholesterolemia	10	50.0	9	45.0	19	47.5
Hypertension	8	20.0	8	20.0	16	40.0
Smoking	6	30.0	6	30.0	12	30.0
Concomitant therapy						
Diuretics	4	20.0	6	30.0	10	25.0
Lipid-lowering drugs	5	25.0	5	25.0	10	25.0
ACEI	4	20.0	5	25.0	9	22.5

(X ± DE) X mean, SD standard deviation, ACEI Angiotensin Converting Enzyme Inhibitors.

All comparisons were not significant

Thirty-nine (39) of 40 included patients (97.5%) completed the 3-month study. One D-003-treated subject withdrew from the study due to a protocol violation. Baseline characteristics of the two study groups were statistically similar, including the OP risk factors (Table 1).

As expected postmenopausal status was the most common risk factor for OP (100%) coherent with enrolment criteria.

Low dietary calcium intake (90%) and personal (85%) or family (70%) history of fractures were also very frequent.

Study patients also exhibited a high frequency of hypercholesterolemia (47.5%), hypertension (40%) and smoking (30%).

Consumption of concomitant therapy was also well matched in both groups.

Efficacy Analysis

According to study protocol, treatment compliance was very good since 39/40 (97.5 %) of study subjects fulfilled that criterion.

Effects on Quality of Life

Table 2 summarizes the effects on QUALEFFO scores. The total QUALEFFO score was significantly ($p<0.0001$ vs baseline, $p<0.05$ vs placebo) improved after D-003 treatment (29.2% versus baseline, 34.5% versus placebo).

In contrast, this value for the placebo increased slightly (5.3%), not significantly. D-003 reduced total QUALEFFO score versus baseline from the first month on treatment, but differences versus placebo were significant only at the end of the study.

In addition, D-003 also reduced significantly QUALEFFO pain, physical activity and health perception scores, while the other scores (social and mental functions) remained unaffected by the treatment.

Effects on Lipid Profile

Serum lipid profile variables were well matched in both groups at randomization (Table 3).

No lipid variable changed significantly in the placebo group. After completing 3 months on therapy, D-003 (10 mg/day) decreased significantly serum LDL-C (17.1%; $p<0.01$ *versus* baseline, $p<0.001$ versus placebo) and TC (8.2%; $p<0.01$ *versus* baseline, $p<0.05$ versus placebo), whereas increased significantly ($p<0.001$ versus baseline and placebo) HDL-C (16.9). TG values, however, were unchanged with D-003.

Safety Profile and Tolerability

Treatment was well tolerated. Four subjects (all from the placebo group) referred some mild AE during the study: heartburn, constipation, headache and high blood pressure.

The only study withdrawal (D-003-treated subject) was due to a protocol violation, not to AE.

Laboratory and physical safety indicators were unaffected by D-003 (Table 4 and 5). Also, individual values remained within normal limits.

Table 2: Effects on QUALEFFO scores (X ± MSE)

	Baseline	1 month	2 months	3 months	Changes (%)
Pain					
D-003	44.2 ± 5.3	25.0 ± 3.3^{++****}	19.5 ± 2.4$^{***+++++}$	14.5 ± 2.6$^{***+++++}$	-67.2
Placebo	47.8 ± 5.6	48.8 ± 5.4	51.0 ± 5.0	53.5 ± 4.6**	+1.1
Physical Activity					
D-003	21.9 ± 2.6	21.7 ± 2.3	12.8 ± 1.6^{****+}	11.9 ± 1.5^{****++}	-45.6
Placebo	19.9 ± 2.9	22.0 ± 3.2	20.9 ± 2.8	21.4 ± 2.8	+7.5
Leisure Activities					
D-003	39.4 ± 3.3	36.5 ± 3.1	35.0 ± 2.8*	35.3 ± 2.9*	-10.4
Placebo	40.3 ± 4.6	38.3 ± 4.8*	39.4 ± 4.3	39.2 ± 4.2	-2.7
General Health perception					
D-003	49.6 ± 5.3	43.3 ± 4.3**	41.7 ± 3.9**	40.8 ± 3.8^{***+}	-17.7
Placebo	45.8 ± 5.3	45.4 ± 5.0	51.3 ± 4.9*	53.8 ± 4.7**	+17.5
Mental status					
D-003	34.9 ± 3.7	33.9 ± 3.6	33.8 ± 3.6	33.6 ± 3.6	-3.7
Placebo	26.8 ± 2.8	26.8 ±2.8	26.9 ± 2.7	26.5 ± 2.9	-1.1
Total Score					
D-003	32.5 ± 2.6	28.1 ± 2.0**	24.1 ± 1.9****	23.0 ± 1.9^{****+}	-29.2
Placebo	30.1 ± 3.0	28.9 ± 2.2	31.2 ± 2.8	31.7 ± 2.8*	+5.3

X mean, MSE mean standard error

*p< 0.05, **p< 0.01, ***p< 0.001, ****p< 0.0001 Comparisons vs baseline (Wilcoxon test for paired samples)

$^{+}$p< 0.05, $^{++}$p< 0.01, $^{+++}$p< 0.001, $^{++++}$p< 0.0001, $^{+++++}$p< 0.00001 Comparisons vs placebo (Mann Whitney U test)

Table 3: Effects on Serum Lipid Profile (mmol/L) (X ± SD)

	Baseline	3 months	Changes (%)
LDL-C (mmol/L)			
D-003	3.56 ± 0.75	2.95 ± 0.49*$^{+++}$	-17.1^{++}
Placebo	3.68 ± 0.81	3.67 ± 0.68	+0.3
Total cholesterol (mmol/L)			
D-003	5.49 ± 0.77	5.04 ± 0.61*+	-8.2^{+++}
Placebo	5.45 ± 0.87	5.54 ± 0.83	+1.7
HDL-C (mmol/L)			
D-003	1.36 ± 0.37	1.59 ± 0.29**$^{+++}$	+16.9^{++++}
Placebo	1.30 ± 0.26	1.25 ± 0.20	-3.8
Triglycerides (mmol/L)			
D-003	1.48 ± 0.56	1.41 ± 0.42	-4.7^{+}
Placebo	1.51 ± 0.66	1.62 ± 0.58	+7.3

(X ± DE) X mean, SD standard deviation,

*p< 0.01, **p< 0.001 Comparisons vs baseline (Wilcoxon test for paired samples)

$^{+}$p< 0.05, $^{++}$p< 0.01, $^{+++}$p< 0.001, $^{++++}$p< 0.0001 Comparisons vs placebo (Mann Whitney U test)

Table 4: Effects on Physical Safety Indicators

	Baseline	1 month	2 months	3 months
Bodyweight (kg)				
D-003	68.97 ± 11.08	69.03 ± 10.92	69.35 ± 10.59	69.23 ± 10.78
Placebo	69.35 ± 11.61	69.75 ± 11.35	69.88 ± 11.33	69.38 ± 11.25
Frequency (beat/min)				
D-003	69.90 ± 2.63	69.90 ± 1.02	69.90 ± 1.21	70.60 ± 1.47
Placebo	70.60 ± 3.73	70.40 ±2.21	70.10 ± 2.10	70.80 ± 1.64
Diastolic blood pressure (mm Hg)				
D-003	77.00 ± 5.48	76.50 ± 4.89	76.50 ± 4.89	76.25 ± 5.35
Placebo	77.00 ± 5.48	76.50 ± 4.89	76.50 ± 4.89	78.50 ± 6.30
Systolic blood pressure (mm Hg)				
D-003	123.25 ± 11.03	122.50 ± 7.69	122.25 ± 8.35	122.50 ± 9.47
Placebo	123.75 ± 11.57	123.75 ± 8.87	125.00 ± 7.78	125.25 ± 10.06

Table 5: Effects on blood biochemical safety indicators

	Baseline	3 months
ALT (U/L)		
D-003	16.70 ± 3.98	16.85 ± 3.30
Placebo	19.80 ± 5.84	19.60 ± 4.20
AST (U/L)		
D-003	18.45 ± 6.68	18.60 ± 5.18
Placebo	21.40 ± 6.95	21.60 ± 4.43
Glucose (mmol/L)		
D-003	4.31 ± 0.43	4.24 ± 0.42
Placebo	4.16 ± 0.51	4.14 ± 0.46
Creatinine (µmol/L)		
D-003	71.35 ± 11.75	71.80 ± 10.69
Placebo	71.70 ± 5.72	70.65 ± 7.36

DISCUSSION

This study demonstrates that D-003 (10 mg/day) administered for short-term (3 months) improved health-based QoL perception in postmenopausal women at moderate to high risk of OP. This affirmation is based on the reductions observed in the total score of QUALEFFO-41, and in the decreases of pain, physical function and health perception QUALEFFO-41 sub-scoring.

The present results are coherent with those found in a previous long-term (3 years) study conducted in a population of postmenopausal women with similar characteristics.[32] Nevertheless, this study reports, for the first time, that such a benefit may be perceived by the women as soon as 3 months after initiating the therapy, which is relevant in terms of their well-being perception. This goal was rationale since evidences that specialized physical treatment for 3 months may improves QoL in activities of daily living in OP.

Nowadays, women may live decades after menopause, but starting in their sixties chronic illnesses, including OP, often affect their quality and span of life. Specifically, in postmenopausal women, the prevalence of OP increase and QoL decreases with lower BMD.[46]

Both study groups were well matched regarding to all baseline characteristics, which supports their homogeneity for comparisons and conclusions. Beyond the postmenopausal status of all study participants, a matter that not only represents an OP risk factor *per se*, but an enrolment criterion that defines the study population, several OP risk factors were also present. Among them, insufficient intake of dietary calcium and personal and familiar previous history of fractures were the most frequent. In addition, it should be noted that study women also displayed a great number of coronary risk factors, consistent with the coexistence of both OP and coronary risk factors in such population subset.[47]

D-003 treatment reduced significantly the total score of QUALEFFO-41 by 34.5% as compared to placebo, which is a meaningful reduction, underlined by the fact that a slight not significant increase (5.3%) of such score, rather than a decrease, was seen in the placebo group. In addition, D-003 reduced significantly QUALEFFO pain, physical activity and health perception scores, which focus on back pain (pain domain), daily living activities, household chores, and mobility (physical function) and on participants' self-assessment of their own QoL (health perception function).

Nevertheless, we believe that the benefits of D-003 on OP-related QoL here seen are not associated to its antiresorptive action since inhibitors of bone resorption given for a longer period (26) weeks did not improve the QoL in postmenopausal women.[48] Also, not all study participants had OP, so that is quite probable that their pain and physical limitations may come from other concomitant complaints present in older women, like joint pain, reduced physical activity, among others.

On its side, D-003 has demonstrated to increase of physical performance and VO2 max of middle aged and elderly subjects subjected to exercise on the static bicycle.[49] The present results are consistent with such facts. In light of these sounds, we cannot discard that beneficial effects of D-003 on the vascular bed may be a reason of the benefits on physical activity found in both studies.

Despite not all participants followed a low fat diet, we found that D-003 (10 mg/day) administered for 3 months, reduced significantly serum LDL-C (secondary outcome), TC and increased HDL-C values, consistent with previous data.[13-19] The cholesterol-lowering effects of D-003 should be seen as an additional benefit in a population with multiple lipid and non-lipid coronary risk factors.

D-003 was very well tolerated. No treated subject referred AE and D-003 did not impair any safety indicator.

These results are in line with previous data of the effects of D-003 (10 mg/day) on postmenopausal women with low BMD. So, administration of D-003 for 6 months reduced significantly the urinary excretion of DPD/creatinine, a marker of bone resorption,[31] and for 3 years increased progressively the lumbar spine BMD and also improved the QoL assessed with QUALEFFO 41.[32] The present results add that benefits of D-003 on QoL of postmenopausal women are perceived faster, which not only makes them feel better more complaint with the treatment.

Evidence-based prevention of OP have to assess the occurrence for OP risk factors in postmenopausal women and to recommend lifestyle management, cessation of smoking, a healthy diet, systematic exercise and reduced alcohol intake. Thus, as part of a strategy to prevent OP after menopause, intake of SCWAc together with the compliment of basic nutritional menopausal may be considered as part of the armamentarium.

CONCLUSION

Short-term (3 months) administration of D-003 (10 mg/day) improved QoL as evidences the significant reduction of total QUALEFFO-41 score and pain, physical function and health perception QUALEFFO-41 scores in postmenopausal women with moderate to high OP risk.

Beside this benefit, D-003 reduced significantly serum LDL-C and TC, while increased HDL-C, changes that should be seen as additional advantages in a population that also exhibits several coronary risk factors.

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