ORIGINAL ARTICLE

Concomitant Use of Policosanol and Commonly Used Drugs in the Elderly Study

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ABSTRACT

Background: Policosanol has been used for more than twenty-five years in Cuban clinical practice and investigated in many clinical studies performed up to date as well as in large surveillance studies. The objective of the present analysis was to determine whether concomitant administration of policosanol with drugs more frequently consumed by elder patients impaired its cholesterol-lowering efficacy or is related to any adverse events occurred during the study. It is also investigated whether administration of policosanol with some concomitant drugs aggravates any particular adverse event. **Materials and Methods:** One thousand ford hundred seventy older patients, between 60 to 80 years old at high coronary risk was recruited, from which 1153 were women and 317 men. The patients were randomized, to policosanol (n=737) or placebo (n=733) and treated during three years. For the present report, the patient records were reviewed, information about concomitant medication were collected and analyzed by Intention-to-treat method. **Results:** Sixty hundred eight patients on policosanol treatment (82.5%) and 597 placebo patients (81.5%) received concomitant drugs. The endpoint analysis by subgroups of concomitant drugs corroborated risk reduction of the primary efficacy endpoint (all-causes serious adverse events) as well as for all cardiovascular and all vascular serious adverse events due to interaction between policosanol with antihypertensive or antiplatelet drugs. Efficacy analysis by subgroups of most consumed drugs did not show any relevant interference with policosanol effect, the efficacy being consistent in all subgroups. After one year on therapy, policosanol reduced low-density lipoprotein-cholesterol (LDL-C) *versus* baseline and placebo in all subgroups. **Conclusion:** These results support the excellent safety profile of policosanol over a long period of treatment, even when it is administered with several concomitant drugs in a population, particularly sensitive to drug-related adverse event and drug/drug interactions, as frequently occurs in the elderly.

Key words: policosanol, elderly, concomitant medications, serious adverse events, cholesterol-lowering.

INTRODUCTION

Coronary disease is the leading cause of morbidity and deaths in adult population. End-point based studies have demonstrated a direct relationship between coronary disease and elevated serum levels of low-density lipoprotein cholesterol (LDL-C) and total cholesterol, as well as the benefits of lowering LDL-C with statins on clinical end-points.[1-3]

Policosanol is a mixture of higher primary aliphatic alcohols purified from sugar cane *(Saccharum officinarum),* was with cholesterol-lowering effects.[4-6] Policosanol inhibit cholesterol synthesis by regulating the activity of hydroxymethylglutaryl coenzyme through the increase of adenosine mono phosphate kinase (AMPK) activity, increasing low-density lipoproteins (LDL) receptor-dependent processing, and catabolic rate of LDL.[7,8] Clinical studies have proven that policosanol is safe and well tolerated[4-6] and no drug-related adverse effects have

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been reported, even in long-term post marketing surveillance studies.[9-11]

The present study was undertaken to determine whether concomitant administration of policosanol with drugs more frequently consumed by older patients induced the increase of some particular adverse event in general or by drug subgroups. Likewise, it is investigated if cholesterol-lowering efficacy was impaired by any of these concomitant drugs as well as if they interfere in the effects of policosanol on the reduction of serious adverse event, main efficacy outcome specified for the whole study.

MATERIALS AND METHODS

The study was conducted according to the principles reflected in the Helsinki statements, as well as the recommendations of the World Health Organization and the Cuban regulations on Good Clinical Practices. The study protocol was approved by the Ministry of Public Health and by the Ethics Committee in Clinical Research of the Medical Surgical Research Centre (Havana, Cuba).

This was a prospective, randomized, double-blinded, placebo-controlled study including 1470 older patients were randomized to policosanol (5 mg) or placebo once a day with evening meal for 36 months.

Older patients of both sexes, aged between 60 and 80 years, were randomized if after the baseline period they showed total cholesterol ≥ 5.2 mmol/L, LDL-C ≥ 3.4 mmol/L and triglycerides < 4.52 mmol/L, if exclusion criteria were not present. Patients were excluded if had active renal or diagnosed neoplastic diseases, severe hypertension, uncontrolled diabetes or poor cognitive function. Patients who had experienced unstable angina, myocardial infarction, stroke or any serious adverse events (SAE) within the three months prior to enrolment were also excluded.

The primary endpoint of the whole study was the combined incidence of fatal + nonfatal SAE from all causes. A SAE was considered any adverse event (AE) leading to patient hospitalization or death, independently of their nature. Secondary endpoints included all mortality and several combined endpoints, such as all fatal + non-fatal coronary, cardiovascular, cerebrovascular and vascular SAE. In the whole study, all events were analyzed according by time of first event. In analyses by subgroup, however, in several cases the sample size and event number was too small for survival and hazard ratio analyses, the groups being compared by relative proportions.

Changes on LDL-C were considered as the secondary efficacy variable. Treatment was considered as effective if LDL-C was significantly reduced by ≥ 15 %,[12] changes on other lipid profile variables (total cholesterol, HDL-C and triglycerides) were also analyzed. In the present analysis we have considered if efficacy was affected in any particular subgroup to explore some possible drug interaction in such regard.

Safety and tolerability analyses included physical (body weight, pulse rate, blood pressure) and laboratory (glucose, creatinine, AST, ALT) safety indicators and tolerability analysis included all data on serious adverse event from nonvascular causes as well as all mild and moderate adverse events.

Blood samples were drawn after 12 hours overnight fasting. Lipid profile and laboratory safety indicators were assessed by enzymatic methods using reagent kits (Roche). Laboratory tests were performed in the Hitachi 719 autoanalyzer (Tokyo, Japan).

All data were analysed according to Intention to-treat principle, so that analyses were based on data of all randomised patients, as randomised. ANOVA was used to compare continuous variables during the study. Comparisons between groups of categorical data were made using Fisher´s Exact Probability test. All statistical tests were two-tailed, with significance at α=0.05. Statistical analyses were performed using Statistica for Windows (Release 4.2; Copyright StatSoft, Inc. US) and SAS/STAT.

RESULTS AND DISCUSSION

The whole prevention study demonstrated the impact of policosanol on clinical outcomes, supporting that lowering LDL-C with policosanol in older hypercholesterolemic patients reduced the risk of all SAE, the primary endpoint, all mortality as well as vascular, cardiovascular and coronary SAE respect to placebo, defined as secondary endpoints. The study also supported the long-term safety of policosanol, which not increased, but surprisingly lowered, the frequency of non-vascular SAE.

The present analysis investigated whether drugs more frequently consumed by study patients impaired cholesterol-lowering efficacy of policosanol or its effects on SAE. The study also investigated whether administration with these concomitant drugs increased some particular AE through the analysis done by drug subgroups.

Of the 1612 patients recruited, 1470 were eligible and randomized to policosanol (n=737) or placebo (n=733). Both groups were well matched at randomization, which support their homogeneity for comparisons (data not shown in Table for simplicity). Most patients were women (1153/1470, 78.4%), 466 (31.7%) were at secondary prevention, while most were at primary prevention at high coronary risk (1004,

68.3%). The mean age of study patients was around 66 years at randomization. The prevalence of hypertension, diabetes and current smoking was 64.1%; 17.9% and 20.2%, respectively.

The frequency of concomitant medications (CM) among study patients was high, 608 policosanol-treated patients (82.5%) and 597 placebo (81.5%) (Table 1). The most frequent concomitant medications are consistent with the risk condition of study population in general and by subgroups and this distribution appears to be consistent with the indications of such drugs.

In the whole study, the frequency of withdrawals in placebo (189, 25.8%) was greater ($p < 0.0001$) than in policosanol group (88, 11.9%). The same was true ($p < 0.0001$) for withdrawals due to adverse event and other reasons, being these last ones mainly related with unsatisfactory efficacy (total cholesterol ≥ 9.0 mmol/L) (data not shown in Table for simplicity).

Effects on clinical end-points: Risk reduction on all-causes SAE was the primary efficacy endpoint of the whole study, in which 109 SAE (fatal + nonfatal) occurred. Of them, there were 83 SAE (11.3%) in placebo and 26 (3.5%) in policosanol group. Policosanol significantly reduced the risk for all-causes SAE, all mortality and all cardiovascular, coronary and vascular SAE with respect to placebo.

The endpoint analysis by subgroups of concomitant drugs corroborated risk reduction of the primary efficacy endpoint (all-causes SAE) as well as for all cardiovascular, coronary and all vascular SAE for the interaction between policosanol and antihypertensive and antiplatelet drugs (Table 2).

In most drug subgroups, the frequency of SAE was lower in policosanol than in respective placebo. The frequency of coronary, cardiovascular and vascular SAE was significantly lower in policosanol than in placebo corresponding to most subgroups.

Table 1. Concomitant medication consumption by study patients

Concomitant medications (CM)*	**Placebo (n = 733)**		**Policosanol (n = 737)**	
Number of CM (X ± SD)	2.4 ± 1		2. 4 ± 1	
	n	**%**	**n**	**%**
Diuretics	181	24.7	187	25.4
Calcium channel blockers	158	21.6	155	21.0
Antiplatelet	173	23.6	161	21.8
Benzodiazepines	118	16.1	121	16.4
β-blockers	107	14.6	98	13.3
Vasodilators	95	13.0	90	12.2
Vitamins	67	9.1	83	11.3
Oral hypoglycemic drugs	79	10.8	65	8.8
Digitalics	37	5.0	42	5.7

X mean, SD standard deviation

*CM consumed by > 5 % of study patients. All comparisons were not significant

The number of deaths in the whole study was actually low, but deaths were less frequent in policosanol than in placebo-treated patients of the subgroups taking calcium channel blockers and vasodilators (data not shown in Table for simplicity).

Cholesterol-lowering efficacy: Table 3 summarizes the effects on lipid profile by subgroups of concomitant therapy. Efficacy analysis by strata of most widely consumed drugs did not show any relevant interference with policosanol effects and the efficacy of policosanol was consistent in all study subgroups.

At study completion LDL-C was significantly lowered by policosanol with respect to baseline and placebo in all subgroups. The mean decreases of LDL-C respect to baseline ranged from 28.7% (subgroup of diuretics) to 35% (subgroup of vasodilators), while decreases on total cholesterol ranged from 19.6% (subgroup of diuretics) to 25% (subgroup of vasodilators). At this time, reductions on triglycerides ranged from 19.3% (subgroup of vasodilators) to 28.7% (subgroup of oral hypoglycemic drugs). HDL-C increased from +13% (subgroup of diuretics) to +18.2% (subgroup of benzodiazepines).

It is important to note that the changes here reported for LDL-C; total cholesterol and HDL-C are consistent with the expected response to policosanol long-term therapy. Reductions on triglycerides for the whole population and study subgroups, however, were superior that in previous studies.[4-6]

Thus, the confirmation of lipid lowering effects of policosanol on such subgroups supports concomitant administration of these drugs with policosanol, without any particular prejudice on its efficacy profile.

Safety and tolerability: In the whole study, policosanol did not increase, but surprisingly reduced the frequency of nonvascular SAE. An analysis by subgroup of concomitant drugs revealed that non vascular SAE were not increased in any group (Table 4).

Policosanol was safe and well tolerated according to the original study as well as analyze by subgroups of concomitant therapy. No drug-related impairment of any safety indicator was observed (data not shown in Table for simplicity). Policosanol, but not placebo, modestly, but significantly reduced systolic blood pressure in all subgroups, while diastolic pressure was also reduced in some subgroups. Such decreases could have contributed to the present results, since lowering systolic pressure significantly reduces coronary events and total mortality in the elderly.[13] The reasons supporting such additive effect on arterial pressure should be related with pleiotropic effects of policosanol, mainly those related with beneficial effects on endothelial function.[14-16]

Frequency of mild+moderate adverse event was similar or lower in policosanol than in placebo by study subgroups. This result, together with SAE and withdrawal analysis, discards any increase in particular adverse event due to policosanol administered with concomitant drugs here reported.

Table 2. Endpoints in study patients taking

	n	%	n	%	p value
Diuretics	**Placebo (n=181)**		**Policosanol (n=187)**		
All SAE (fatal + non fatal)	23	12.7	9	4.8	p < 0.01
All vascular SAE	17	9.4	5	2.7	p < 0.01
All cardiovascular SAE	13	7.2	2	1.1	p < 0.01
All coronary SAE	12	6.6	2	1.1	p < 0.01
Calcium channel blckers	**Placebo (n= 158)**		**Policosanol (n = 155)**		
All SAE (fatal + non fatal)	24	15.2	4	2.6	p < 0.001
All vascular SAE	16	10.1	3	1.9	p < 0.001
All cardiovascular SAE	12	7.6	1	0.6	p < 0.01
All coronary SAE	11	6.7	1	0.6	p < 0.01
Antiplatelets	**Placebo (n= 173)**		**Policosanol (n = 161)**		
All SAE (fatal + non fatal)	23	16.8	10	6.8	p < 0.01
All vascular SAE	16	12.1	8	5.0	p < 0.01
All cardiovascular SAE	11	8.7	2	1.2	p < 0.05
All coronary SAE	10	8.1	2	1.2	p < 0.05
Benzodiazepines	**Placebo (n= 118)**		**Policosanol (n = 121)**		
All SAE (fatal + non fatal)	10	8.5	6	5.0	ns
All vascular SAE	5	4.2	3	2.5	ns
All cardiovascular SAE	4	3.4	1	0.8	ns
All coronary SAE	4	3.4	1	0.8	ns
β-blockers	**Placebo (n= 107)**		**Policosanol (n = 98)**		
All SAE (fatal + non fatal)	15	14.0	3	3.1	p < 0.01
All vascular SAE	11	8.4	3	3.1	p < 0.05
All cardiovascular SAE	8	5.6	0	0.0	p < 0.01
All coronary SAE	8	5.6	0	0.0	p < 0.01

Vasodilators	**Placebo (n= 95)**		**Policosanol (n = 90)**		
All SAE (fatal + non fatal)	22	23.2	3	3.3	$p < 0.01$
All vascular SAE	15	15.8	3	3.3	$p < 0.01$
All cardiovascular SAE	13	13.7	2	2.2	$p < 0.01$
All coronary SAE	13	13.7	2	2.2	$p < 0.01$
Vitamins	**Placebo (n= 67)**		**Policosanol (n = 83)**		
All SAE (fatal + non fatal)	5	7.5	2	2.4	ns
All vascular SAE	3	4.5	2	2.4	ns
All cardiovascular SAE	3	4.5	2	2.4	ns
All coronary SAE	2	3.0	2	2.4	ns
Oral hypoglycemic drugs	**Placebo (n= 79)**		**Policosanol (n = 65)**		
All SAE (fatal + non fatal)	18	22.8	1	1.5	$p < 0.0001$
All vascular SAE	13	16.4	1	1.5	$p < 0.001$
All cardiovascular SAE	7	8.9	0	0.0	$p < 0.01$
All coronary SAE	7	8.9	0	0.0	$p < 0.01$
Digitalics	**Placebo (n= 37)**		**Policosanol (n = 42)**		
All SAE (fatal + non fatal)	10	27.0	3	7.1	$p < 0.05$
All vascular SAE	5	13.5	2	4.8	ns
All cardiovascular SAE	3	8.1	0	0.0	ns
All coronary SAE	3	8.1	0	0.0	ns

SAE (serious adverse events), Patients are counted only once with a specific endpoint, but they may be listed more than once because of experiencing an event included in more than one endpoint. Comparison with placebo, Fisher´s Exact Probability Test

Table 3A. Long-term effects of policosanol on lipid profile (X±SD) of study patients taking

Study groups	**Baseline**	**1 year**	**2 years**	**3 years**
Diuretics		**Total cholesterol (mmol/L)**		
Policosanol	6.69 ± 0.83	5.43 ± 6.63^{+++}	5.26 ± 0.57^{+++}	5.38 ± 0.72^{+++}
Placebo	6.63 ± 0.84	6.68 ± 0.86	6.70 ± 0.80	6.70 ± 0.83
		LDL-C (mmol/L)		
Policosanol	4.70 ± 0.83	3.70 ± 0.64^{+++}	3.43 ± 0.63^{+++}	3.35 ± 0.64^{+++}
Placebo	4.67 ± 0.85	4.67 ± 0.88	4.76 ± 0.81	4.70 ± 0.81
		HDL-C (mmol/L)		
Policosanol	1.23 ± 0.34	1.28 ± 0.23^{++}	1.37 ± 0.28^{+++}	1.39 ± 0.24^{+++}
Placebo	1.21 ± 0.29	1.17 ± 0.28	1.19 ± 0.18	1.17 ± 0.19
		Triglycerides (mmol/L)		
Policosanol	2.32 ± 1.01	1.82 ± 0.66^{+++}	1.87 ± 0.65^{++}	1.82 ± 0.56^{+}
Placebo	2.31 ± 1.15	2.32 ± 0.99	2.33 ± 0.62	2.40 ± 0.54
Calcium channel blockers		**Total cholesterol (mmol/L)**		
Policosanol	6.82 ± 0.86	5.40 ± 0.61^{++++}	5.36 ± 0.62^{++++}	5.26 ± 0.62^{++++}
Placebo	6.85 ± 0.96	6.78 ± 0.99	6.78 ± 0.95	6.70 ± 0.93

LDL-C (mmol/L)				
Policosanol	4.80 ± 0.90	3.76 ± 0.63^{++++}	3.39 ± 0.60^{++++}	3.28 ± 0.63^{++++}
Placebo	4.74 ± 0.93	4.74 ± 0.90	4.80 ± 0.93	4.64 ± 0.98
HDL-C (mmol/L)				
Policosanol	1.16 ± 0.31	1.27 ± 0.26	1.31 ± 0.26^{++++}	1.36 ± 0.24^{++++}
Placebo	1.19 ± 0.35	1.20 ± 0.32	1.15 ± 0.27	1.14 ± 0.21
Policosanol	2.35 ± 0.95	1.84 ± 0.64	1.84 ± 0.46	1.87 ± 0.57
Placebo	2.32 ± 1.12	2.22 ± 0.90	2.22 ± 0.67	2.16 ± 0.45
Antiaggregants	**Total cholesterol (mmol/L)**			
Policosanol	6.85 ± 0.93	5.34 ± 0.52^{++++++}	5.21 ± 0.53^{++++++}	5.21 ± 0.56^{++++++}
Placebo	6.65 ± 0.89	6.62 ± 0.91	6.57 ± 0.78	6.48 ± 0.82
LDL-C (mmol/L)				
Policosanol	4.75 ± 0.88	3.75 ± 0.73^{++++++}	3.33 ± 0.59^{++++++}	3.12 ± 0.56^{++++++}
Placebo	4.63 ± 0.86	4.62 ± 0.83	4.76 ± 0.84	4.68 ± 0.79
HDL-C (mmol/L)				
Policosanol	1.24 ± 0.35	1.28 ± 0.24^{+}	1.34 ± 0.25^{+}	1.42 ± 0.23^{++++++}
Placebo	1.22 ± 0.33	1.18 ± 0.30	1.19 ± 0.23	1.19 ± 0.14
Triglycerides (mmol/L)				
Policosanol	2.30 ± 0.88	1.85 ± 0.70^{+}	1.83 ± 0.35^{+}	1.79 ± 0.34^{+}
Placebo	2.22 ± 1.03	2.10 ± 0.73	2.09 ± 0.59	2.09 ± 0.56
Benzodiazepines	**Total cholesterol (mmol/L)**			
Policosanol	6.82 ± 0.90	5.38 ± 0.58^{+++}	5.29 ± 0.68^{+++}	5.35 ± 0.76^{+++}
Placebo	6.67 ± 0.87	6.63 ± 0.88	6.62 ± 0.73	6.64 ± 0.71
LDL-C (mmol/L)				
Policosanol	4.80 ± 0.83	3.78 ± 0.73^{+++}	3.40 ± 0.60^{+++}	3.31 ± 0.72^{+++}
Placebo	4.66 ± 0.84	4.64 ± 0.81	4.74 ± 0.90	4.71 ± 0.71
HDL-C (mmol/L)				
Policosanol	1.18 ± 0.35	1.30 ± 0.28	1.31 ± 0.25^{+++}	1.39 ± 0.24^{+++}
Placebo	1.20 ± 0.34	1.23 ± 0.32	1.18 ± 0.18	1.18 ± 0.12
Triglycerides (mmol/L)				
Policosanol	2.26 ± 0.93	1.78 ± 0.60^{++}	1.76 ± 0.46^{+++}	1.74 ± 0.22^{+++}
Placebo	2.14 ± 0.79	2.05 ± 0.66	2.13 ± 0.70	2.11 ± 0.59
ß-blockers	**Total cholesterol (mmol/L)**			
Policosanol	6.77 ± 1.01	5.46 ± 0.66^{+++}	5.22 ± 0.56^{+++}	5.20 ± 0.62^{+++}
Placebo	6.78 ± 0.84	6.79 ± 0.81	6.78 ± 0.78	6.72 ± 0.78

LDL-C (mmol/L)				
Policosanol	4.69 ± 1.04	3.71 ± 0.63^{+++}	3.38 ± 0.63^{+++}	3.08 ± 0.43^{+++}
Placebo	4.70 ± 0.88	4.73 ± 0.76	4.73 ± 0.78	4.85 ± 0.78
HDL-C (mmol/L)				
Policosanol	1.22 ± 0.35	1.27 ± 0.24^{++}	1.35 ± 0.27^{+++}	1.37 ± 0.23^{+++}
Placebo	1.24 ± 0.32	1.16 ± 0.23	1.17 ± 0.19	1.18 ± 0.17
Triglycerides (mmol/L)				
Policosanol	2.41 ± 0.10	2.22 ± 0.52^{+++}	1.88 ± 0.77^{+}	1.90 ± 0.86
Placebo	2.31 ± 0.93	2.37 ± 0.80	2.39 ± 0.50	2.37 ± 0.38
Vasodilators	**Total cholesterol (mmol/L)**			
Policosanol	6.80 ± 0.96	5.38 ± 0.57^{++++++}	5.26 ± 0.56^{++++++}	5.10 ± 0.27^{++++++}
Placebo	6.69 ± 0.80	6.73 ± 0.86	6.69 ± 0.68	6.52 ± 0.85
LDL-C (mmol/L)				
Policosanol	4.83 ± 0.86	3.82 ± 0.68^{++++++}	3.42 ± 0.61^{++++++}	3.11 ± 0.31^{++++++}
Placebo	4.59 ± 0.84	4.61 ± 0.85	4.81 ± 0.81	4.61 ± 0.84
HDL-C (mmol/L)				
Policosanol	1.20 ± 0.32	1.27 ± 0.17	1.31 ± 0.23^{++}	1.42 ± 0.21^{++++++}
Placebo	1.21 ± 0.32	1.19 ± 0.24	1.18 ± 0.28	1.18 ± 0.20
Triglycerides (mmol/L)				
Policosanol	2.18 ± 0.79	1.76 ± 0.50^{+++}	1.79 ± 0.30^{++++++}	1.76 ± 0.19^{++++++}
Placebo	2.26 ± 1.08	2.21 ± 0.75	2.11 ± 0.59	2.20 ± 0.52
Vitamins	**Total cholesterol (mmol/L)**			
Policosanol	6.81 ± 0.85	5.39 ± 0.66^{+++}	5.27 ± 0.66^{++++}	5.33 ± 0.74^{++++++}
Placebo	6.56 ± 0.79	6.56 ± 0.80	6.53 ± 0.75	6.48 ± 0.75
LDL-C (mmol/L)				
Policosanol	4.73 ± 0.91	3.59 ± 0.67^{+++}	3.31 ± 0.60^{++++}	3.22 ± 0.70^{++++++}
Placebo	4.54 ± 0.89	4.51 ± 0.95	4.61 ± 0.80	4.63 ± 0.77
HDL-C (mmol/L)				
Policosanol	1.21 ± 0.32	1.28 ± 0.24^{++}	1.36 ± 0.29^{+++}	1.43 ± 0.28^{++++}
Placebo	1.18 ± 0.29	1.16 ± 0.30	1.17 ± 0.18	1.16 ± 0.17
Triglycerides (mmol/L)				
Policosanol	2.28 ± 0.79	1.79 ± 0.49^{++}	1.81 ± 0.34^{++}	1.80 ± 0.24^{++}
Placebo	2.31 ± 1.13	2.25 ± 0.77	2.24 ± 0.54	2.26 ± 0.68
Oral hypoglycemic drugs	**Total cholesterol (mmol/L)**			
Policosanol	6.81 ± 0.90	5.30 ± 0.45^{+++}	5.20 ± 0.44^{+++}	5.12 ± 0.36^{+++}
Placebo	6.73 ± 0.89	6.63 ± 0.91	6.57 ± 0.82	6.70 ± 0.75

LDL-C (mmol/L)				
Policosanol	4.56 ± 0.84	3.57 ± 0.87^{+++}	3.21 ± 0.48^{+++}	3.07 ± 0.35^{+++}
Placebo	4.57 ± 0.88	4.61 ± 0.89	4.72 ± 0.87	4.77 ± 0.75
HDL-C (mmol/L)				
Policosanol	1.25 ± 0.34	1.32 ± 0.23	1.35 ± 0.27^{+++}	1.37 ± 0.20^{+++}
Placebo	1.22 ± 0.31	1.18 ± 0.35	1.16 ± 0.17	1.15 ± 0.21
Triglycerides (mmol/L)				
Policosanol	2.71 ± 0.90	2.03 ± 0.73^{+}	1.93 ± 0.37^{+++}	1.85 ± 0.31^{+++}
Placebo	2.69 ± 1.17	2.72 ± 1.22	2.74 ± 0.57	2.67 ± 0.67
Digitalics	**Total cholesterol (mmol/L)**			
Policosanol	6.76 ± 1.08	5.39 ± 0.65	5.24 ± 0.52^{++}	5.13 ± 0.45^{+++}
Placebo	6.52 ± 0.88	6.54 ± 1.07	6.35 ± 0.66	6.45 ± 0.71
LDL-C (mmol/L)				
Policosanol	4.60 ± 1.05	3.60 ± 0.67^{+++}	3.35 ± 0.73^{+++}	3.10 ± 0.41^{+++}
Placebo	4.55 ± 0.85	4.46 ± 0.94	4.60 ± 0.89	4.51 ± 0.70
HDL-C (mmol/L)				
Policosanol	1.20 ± 0.39	1.30 ± 0.26^{+}	1.34 ± 0.34^{++}	1.40 ± 0.29^{++}
Placebo	1.21 ± 0.33	1.19 ± 0.33	1.19 ± 0.18	1.18 ± 0.08
Triglycerides (mmol/L)				
Policosanol	2.54 ± 1.02	2.03 ± 0.78	1.99 ± 0.38	1.91 ± 0.36
Placebo	2.51 ± 1.29	2.39 ± 0.96	2.37 ± 0.58^{+}	2.41 ± 0.88^{+}

X mean, SD standard deviation

$^{+}p < 0.05$; $^{++}p < 0.01$; $^{+++}p < 0.001$, $^{++++}p < 0.0001$,$^{+++++}p < 0.00001$ ANOVA

Table 4. Non-vascular SAE of study patients taking

Concomitant drugs	Placebo	Policosanol	p value
Diuretics	6	4	ns
Calcium channel blockers	8	1	p<0.05
Antiplatelet	7	2	p<0.05
Benzodiazepines	5	3	ns
β-blockers	4	0	ns
Vasodilators	7	0	p<0.05
Vitamins	2	0	ns
Oral hypoglycemic drugs	5	2	ns
Digitalics	0	0	ns

SAE serious adverse events, *Comparison with placebo (Fisher's Exact Probability test)

CONCLUSION

These results support that policosanol has an excellent long-term safety profile, even when it is administered with several concomitant drugs in a population particularly sensitive to drug-related adverse event and drug/drug interactions, as occurs in the elderly.

CONPLIANCE WITH ETHICAL STANDARDS

Financial Disclosure: This study was support by the National Centre for Scientific Research, as part of its research-development projects.

Conflict of interest: The authors declare that there is no conflict of interest in relation to this work.

Statement of informed consent: Informed consents was obtained from all individual participants include in the study.

REFERENCES

1. Gidding S.S. and Allen N.B. Cholesterol and Atherosclerotic Cardiovascular Disease: A Lifelong Problem. J. Am. Heart Assoc. 8(11), e012924 (2019).
2. Kazi D.S., Penko J.M. and Bibbins-Domingo K. Statins for primary prevention of cardiovascular disease: Review of Evidence and Recommendations for Clinical Practice. Med. Clin. North Am. 101(4), 689 (2017).
3. Jellinger P.S., Handelsman Y., Rosenblit P.D., Bloongarden Z.T., Fonseca V.A. and Garber A.J. American association of Clinical Endocrinologists and American College of Endocrinology. Guidelines for management of dyslipidemia and prevention of cardiovascular disease. Endocrine Practice. 23(2), 1 (2017).
4. Mas R. Policosanol Drugs of the Future. 25, 569 (2000).
5. Castaño G., Más R., Fernández J.C., Illnait J., Fernandez L. and Alvarez E. Effects of policosanol in older patients with type II hypercholesterolemia and high coronary risk. J. Gerontol. Sci. Med. Sci. 56(3), M186 (2001).
6. Mas R., Castaño G., Fernández L., Illnait J., Fernandez J.C. and Alvarez E. Effects of policosanol in older hypercholesterolemic patients with coronary disease. Clin. Drug Invest. 21, 485 (2001).
7. Sing D.K., Li Li. and Poter T.D. Policosanol inhibits cholesterol synthesis in hepatoma cells by activation of AMP-kinase. J. Pharmacol. Ther. 318, 1020 (2006).
8. Banerjee S., Ghoshal S. and Porter T.D. Activation of AMP-kinase by policosanol requires peroxisomal metabolism. Lipids. 46(4), 311 (2011).
9. Fernández L, Más R, Illnait J, Fernández JC. Policosanol: results of a postmarketing surveillance control on 27 879 cases. Curr. Ther. Res. 59, 717 (1998).
10. Más R., Rivas P., Izquierdo J.E., Hernández R., Fernández L., Fernández J.C., Orta S.D., Illnait J. and Ricardo Y. Pharmacoepidemiologic study of policosanol. Curr. Ther. Res. 60, 458 (1999).
11. Fernández S., Mas R., Gamez R., Díaz A., Fernández J., Orta S.D., Illnait J., Castaño G., Mendoza S., Valdes F. and Alvarez E. A pharmacological surveillance of policosanol tolerability in the elderly. Am. J. Ger. Pharmacotherapy. 2, 219 (2004).
12. Karalis D.G., Subramanya R.D., Hessen S.E., Liu L. and Victor M.F. Achieving optimal lipid goals in patients with coronary artery disease. Am. J. Cardiol. 107(6), 886 (2011).
13. Denker M.G., Cohen D.L. What is an appropriate blood pressure goal for the elderly: review of recent studies and practical recommendation. Clin. Interv. Aging. 8, 1505 (2013).
14. Lee E.Y., Yoo J.A., Lim S.M. and Cho K.H. Anti-aging and tissue regeneration ability of policosanol along with lipid-lowering effect in hyperlipidemic zebrafish via enhancement of high-density lipoprotein functionality. Rejuvenation Research. 19(2), 149 (2016).
15. Kim S.J, Yadav D., Park H.J., Kim J.R. and Cho K.H. Long-term consumption of Cuban policosanol lowers central and brachial blood pressure and improves lipid profile with enhancement of lipoprotein properties in healthy Korean participants. Front. Physiol. 9, 412 (2018).
16. Kim J.Y., Kim S.M., Kim S.J., Lee E.Y., Kim J.R. and Cho K.H. Consumption of policosanol enhances HDL functionality via CETP inhibition and reduces blood pressure and visceral fat in young and middle-aged subjects. International Journal of Molecular Medicine. 39(4), 889 (2017).

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