Effects of a policosanol supplement on serum lipid concentrations in hypercholesterolaemic and heterozygous familial hypercholesterolaemic subjects

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Policosanol is a mixture of higher aliphatic primary alcohols that is extracted from purified sugar cane wax or a variety of other plant sources, and has been shown to have beneficial effects on serum lipid concentrations. The objective of this study was to investigate the effects of a policosanol supplement (Octa-60) on lipid profiles of hypercholesterolaemic and heterozygous familial hypercholesterolaemic subjects. Nineteen hypercholesterolaemic and familial hypercholesterolaemic subjects completed this randomised, placebo-controlled, double-blind study. The subjects received either a daily dose of 20 mg policosanol or placebo for 12 weeks. After a wash-out period of 4 weeks, the interventions were crossed over. Lipid levels were measured at baseline and at the end of each intervention period. No significant differences in total cholesterol and LDL-cholesterol from baseline to end or between policosanol and placebo were seen in the hypercholesterolaemic or familial hypercholesterolaemic groups. There were small reductions in total cholesterol and LDL-cholesterol from baseline to end in the hypercholesterolaemic group, but these changes did not differ significantly from the changes with the placebo, indicating that the observed decrease in cholesterol in the policosanol group was not due to the specific effect of policosanol treatment. The differences in response may be ascribed to the differences in composition of the higher aliphatic primary alcohols in the previously used products, compared with the local policosanol supplement. An intake of 20 mg/d policosanol for 12 weeks had no significant effect on serum lipid levels in hypercholesterolaemic and heterozygous familial hypercholesterolaemic patients when compared with placebo intake.

Policosanol: Lipids: Cholesterol: Familial hypercholesterolaemia

Policosanol is a natural mixture of higher aliphatic primary alcohols, extracted from purified sugar cane wax (*Saccharum officinarum* L.) by hydrolytic cleavage and subsequent purification. The mixture can also be obtained from a variety of other plant sources as well as beeswax. The major components of the mixture are octacosanol (60–70 %w/w), triacocontanol (10–15 %w/w) and hexacosanol (4·5–10 %w/w), with tetracosanol, heptacosanol, nonacosanol, dotriacontanol and tetratriacontanol making up the lesser constituents (Mas, 2000).

Numerous well-designed clinical studies have shown highly beneficial effects of policosanol on serum lipid levels. Studies on hypercholesterolaemic patients have shown that 10 mg policosanol per day significantly lowered total cholesterol by between 14·1 and 18 %, and LDL-cholesterol (LDL-C) by between 21·1 and 27·5 %, while raising HDL-cholesterol (HDL-C) by 11·2–28·9 % (Pons *et al.* 1994; Aneiros *et al.* 1995; Canetti *et al.* 1995; Castano *et al.* 1997, 2002*c*). Policosanol has also shown similar efficacy in patients with type II diabetes (Torres *et al.* 1995; Crespo *et al.* 1997; Castano *et al.* 2003*a*) and in a number of animal models (Arruzazabala *et al.* 1994; Rodriguez-Echenique *et al.* 1994; Menendez *et al.* 1997). Policosanol appears to act in a dose-dependent manner (Janikula, 2002).

Of special interest in judging the efficacy of policosanol are trials in which the effects of established lipid-lowering medications, in this case statins, were compared with those of policosanol. A comparison of pravastatin (Benitez *et al.* 1997), lovastatin (Castano *et al.* 2000*a*; Crespo *et al.* 1999) and fluvastatin (Fernandez *et al.* 2001) against policosanol, in comparable dosages, showed that statins and policosanol lowered the total cholesterol to the same extent, whereas the decrease in LDL-C and the increase in HDL-C were more pronounced with policosanol treatment.

Toxicological studies in rats have shown that doses as high as 500 mg/kg body weight, which is 1724 times the recommended therapeutic dose, resulted in no reports of toxicity (Aleman *et al.* 1994). Doses of up to 5000 mg/kg did not show any evidence of oral toxicity (Gamez *et al.* 2001). Similarly, studies on carcinogenicity (Aleman *et al.* 1994, 1995), reproduction and teratogenicity (Rodriguez & Garcia, 1994, 1998) did not show any adverse effects.

Most of the clinical studies on policosanol were, however, conducted at a limited number of centres. Thus, there is a need for the current data on policosanol to be confirmed by other laboratories in different populations (Gouni-Berthold & Berthold, 2002; Janikula, 2002; Lin *et al.* 2004).

The efficacy of policosanol in lowering LDL-C in familial hypercholesterolaemia has not yet been tested. These subjects present a major genetic dominant disorder caused by a mutation in the LDL receptor gene, resulting in elevated blood cholesterol concentrations and risk of CHD. The objective of this study was therefore to investigate the effects of a policosanol supplement (Octa-60; Garuda International Inc. Lemon cove, CA, USA; purified from sugar cane wax) on the serum lipid profiles of hypercholesterolaemic subjects and heterozygous subjects with familial hypercholesterolaemia.

Methods

Subjects

This study was conducted at the Lipid Clinic of the School of Physiology, Nutrition and Consumer Sciences of the North-West University, South Africa. Ethical approval to conduct the study was obtained from the ethical committee of the university (ethics no: 03M06).

Men and women were eligible to participate if they met the following criteria: age older than 21 years and with a serum total cholesterol concentration above 5 mmol/l. Heterozygous familial hypercholesterolaemic subjects had to have a LDL receptor mutation on exon 4 or 9 of the LDL receptor gene or had to meet the diagnostic criteria for determining familial hypercholesterolaemia as stipulated by Defesche (Sauvage Nolting et al. 2003). Exclusion criteria included serum triacylglycerol levels above 2·5 mmol/l, being a smoker, pregnancy or lactation, the use of anticoagulant medication or the use of aspirin in excess of 300 mg/d.

Subjects using lipid-lowering medication (specifically statins) were included in the study for ethical reasons. Because of the very high total cholesterol and LDL-C concentrations in familial hypercholesterolaemic patients, almost all heterozygous familial hypercholesterolaemic patients need to take lipid-lowering medication to reach their target LDL-C levels (Civeira 2004). It is therefore not feasible to obtain a large subject group who are not using statins, and we viewed it as unethical to require subjects to discontinue their statin treatment. Subjects using statins had to have been stable on the medication for at least 3 months prior to inclusion in the study. They were instructed not to change their dosage or treatment regimen in any way for the duration of the study, and they had to comply with the inclusion criteria: namely, they had to have an increased total cholesterol concentration while using statins.

Forty-four hypercholesterolaemic (twenty-two of whom were familial hypercholesterolaemic) volunteers who regularly attend the lipid clinic were recruited as based on a power calculation using total cholesterol (Margetts & Nelson, 1997), as measured in this population. Based on an expected LDL-C-lowering effect of at least 20 % (Castano et al. 2002b, 2003c), this number of subjects would have provided at least 80 % power at a 5 % level of significance. The subjects signed informed consent forms for participation in the study. The baseline characteristics of the subjects can be seen in Table 1.

Upon enrolment at the lipid clinic, all the subjects received dietary counselling regarding a dyslipidaemic diet (55 % energy as carbohydrates, 15 % as protein and 30 % as fat, with less than 10 % energy intake in the form of saturated fat and less than 300 mg/d cholesterol) from a registered dietician, along with other lifestyle recommendations. All of the subjects had been attending the lipid clinic for at least 3 months, had a stable weight and were following their individually adapted diets as their normal routine.

Each subject received a calendar with important dates (e.g. when blood would be taken, etc.). They were asked to maintain their normal daily routine (eating pattern, physical activity, alcohol consumption) for the duration of the study. The subjects were also asked to keep a diary of illnesses and any changes in medication used (if absolutely necessary) during the study.

Subjects were asked to report any adverse effects. Adverse events were defined as 'mild' if cessation of the study treatment was not required and 'moderate' if a physician recommended specific treatment and/or discontinuation of the study treatment. Serious adverse events were defined as those being fatal or leading to prolonged hospitalisation.

Table 1. Subjects' baseline characteristics

Characteristics	Familial hypercholesterolaemia		Hypercholesterolaemia	
	Mean	95 % CI	Mean	95 % CI
Male	2		13	
Female	14		6	
Age (years)	47	41·6,52·4	51·1	46·2,56·0
Weight (kg)	72	65·2,78·5	88	81·9,93·9
Height (m)	1·64	1·58,1·69	1·74	1·70,1·78
BMI (kg/m^2)	26·75	24·7,28·8	29·1	27·2,31·0
Serum total cholesterol (mmol/l)	6·84	6·03,7·65	6·37	5·94,6·80
Serum HDL-C (mmol/l)	1·16	1·03,1·29	1·09	0·97,1·21
Serum LDL-C (mmol/l)	5·20	4·31,6·09	4·34	3·99,4·69
Serum triacylglycerol (mmol/l)	1·31	0·89,1·73	1·92	1·55,2·30
Statin use:	n 10		n 3	
5 mg	n 1		n 1	
10 mg	n 0		n 1	
20 mg	n 8		n 1	
40 mg	n 1		n 0	

HDL-C, HDL-cholesterol; LDL-C, LDL-cholesterol.

Study design and protocol

A randomised, placebo-controlled, double-blind, crossover study design was employed for this study.

Volunteers meeting the selection criteria were first divided into two groups (hypercholesterolaemic and familial hypercholesterolaemic) and then paired off according to use of lipid-lowering medication. The respective groups were then randomly assigned to either the active treatment or placebo using random numbers tables. Each treatment period lasted 12 weeks, with a washout period of 4 weeks employed between the two treatment periods.

Anthropometric measurements were taken before and every 3 weeks during the intervention period. BMI (kg/m^2) was calculated.

Supplements and placebos

The policosanol supplement contained 20 mg of the higher aliphatic primary alcohol mixture (purified from sugar cane wax) Lesstanol Octa-60 as the active ingredient as well as 400 μg folic acid, and was supplied by MZL Investments cc (Cape Town, South Africa). The placebo was identical to the supplement but consisted of corn starch as well as 400 μg folic acid. Subjects received one tablet per day of either the supplement or the placebo, which was taken after the evening meal owing to greater synthesis of cholesterol at night (Pappu & Illingworth, 2002; Siavoshian *et al.* 1995).

Blood samples

A qualified nursing sister, using a 21-gauge scalp infusion set, collected venous blood samples after a 12 h overnight fast. Samples were drawn with minimum stasis between 07.00 and 10.00 hours to avoid the effects of diurnal variation. A 10 ml blood sample was drawn and left to clot, after which the blood was centrifuged at 4000 rpm for 15 min at 10°C to yield serum for lipid analysis. Serum was divided into aliquots and stored at −82°C until analysis. Serum triacylglycerol, total cholesterol and HDL-C were measured using a Vitros DT60 II Chemistry Analyser (Ortho-Clinical Diagnostics, Rochester, NY, USA). Serum LDL-C was calculated using the formula of Friedewald *et al.* (1972).

Compliance

Compliance was determined by pill-counting. A dose of three, five or seven tablets were randomly added to each subject's given amount (twenty-one tablets every 3 weeks). This extra amount was recorded next to each subject's identity number on the file. Every 3 weeks, the left-over tablets were counted and compared with the number on file. Subjects were then interviewed and supplied with tablets for the next 3 weeks.

Statistical analysis

The computer software package Statistica (StatSoft® Ltd, Bedford, UK) was used for the statistical analysis. The variables were tested for normality using the Shapiro Wilk test. Significant differences within groups (from baseline to end) and between groups that were normally distributed were determined with the *t* test for dependent variables. These variables are presented as means and 95 % CI. A *P* value ⩽ 0·05 was regarded as statistically significant. A nested-design ANOVA was used to determine whether the order of policosanol or placebo treatment influenced the results. Analysis of covariance was used to analyse the effects of treatment on changes in variables while controlling for the effects of baseline lipid concentrations and changes in BMI.

Results

The responses in terms of lipid variables for men and women did not differ from each other and always occurred in the same direction. The data were therefore analysed and reported for men and women combined. Data from the familial hypercholesterolaemic and hypercholesterolaemic groups are reported separately. There were no order-of-treatment effects.

Dropouts

Nine subjects were not included in the final statistical analysis; six were familial hypercholesterolaemic and three were hypercholesterolaemic. Two subjects changed the type of lipid-lowering medication they were using, and one subject stopped using statins. One subject started hormone replacement therapy. One subject's triacylglycerol levels rose above exclusion criteria values, possibly owing to weight gain. One subject's weight increased by 4·6 kg during the placebo phase, and three subjects abandoned the study for personal reasons. There was no indication that these subjects were in any way different from those who completed the study.

Compliance

Overall compliance with policosanol pill intake during the study was very good. Estimations of compliance for the two groups were 94·03 % for the supplement and 90·44 % for the placebo in the familial hypercholesterolaemic group, and 91·48 % for the supplement and 94·87 % for the placebo in the hypercholesterolaemic group.

Safety and tolerability

Four adverse events were reported during the study. All were classified as mild events, and no patient withdrew from the study because of adverse events. Three of the events, which included two cases of headache and one case of vertigo, were reported during policosanol intake. One adverse event (fluid retention) was reported with the placebo treatment. Similar adverse events have been reported in other studies. In all cases, however, these events involved less than 1 % of the population (Fernandez *et al.* 1998; Mas *et al.* 1999*b*). It therefore seems highly unlikely that the adverse events can be ascribed to the use of the policosanol supplement.

Effects of policosanol on serum lipid levels

Changes in serum lipid levels and body weight are summarised in Table 2 for the familial hypercholesterolaemic group and Table 3 for the hypercholesterolaemic group. There was a statistically significant increase of 0·27 kg/m^2 BMI and

Table 2. Mean (95 % CI) changes in familial hypercholesterolaemic subjects (*n* 16)

Variable	Policosanol		P value (difference within group)	Placebo		P value (difference within group)	P value(difference between groups)
	Mean	95 % CI		Mean	95 % CI		
Weight (kg)							
Baseline	71·58	65·22,77·95	0·002	71·83	65·2,78·45	0·31	
End	72·33	65·80,78·85		72·15	65·48,78·83		
Baseline − end	0·74	0·32,1·16		0·33	−0·34,1·00		0·36
BMI (kg/m²)							
Baseline	26·68	24·65,28·71	0·002	26·75	24·70,28·79	0·29	
End	26·95	24·88,29·02		26·88	24·77,28·98		
Baseline − end	0·27	0·11,0·42		0·13	−0·13,0·39		0·42
Total cholesterol (mmol/l)							
Baseline	7·14	6·18,8·09	0·72	6·84	6·03,7·65	0·44	
End	7·21	6·26,8·15		7·07	6·11,8·03		
Baseline − end	0·07	−0·34,0·49		0·23	−0·39,0·85		0·67
HDL-C (mmol/l)							
Baseline	1·22	1·10,1·34	0·58	1·16	1·03,1·29	0·35	
End	1·25	1·08,1·41		1·19	1·06,1·32		
Baseline − end	0·03	−0·09,0·15		0·03	−0·04,0·11		0·97
LDL-C (mmol/l)							
Baseline	5·30	4·34,6·27	0·47	5·20	4·31,6·09	0·88	
End	5·47	4·56,6·38		5·25	4·26,6·23		
Baseline − end	0·16	−0·31,0·64		0·05	−0·62,0·71		0·77
Triacylglycerol (mmol/l)							
Baseline	1·43	0·92,1·94	0·14	1·31	0·89,1·73	0·88	
End	1·29	0·89,1·68		1·32	0·93,1·71		
Baseline − end	−0·14	−0·34,0·06		0·01	−0·17,0·19		0·16

HDL-C, HDL-cholesterol; LDL-C, LDL-cholesterol.

Table 3. Mean (95 % CI) changes in hypercholesterolaemic subjects (*n* 19)

Variable	Policosanol		P value (difference within group)	Placebo		P value (difference within group)	P value (difference between groups)
	Mean	95 % CI		Mean	95 % CI		
Weight (kg)							
Baseline	88·14	82·08,94·21	0·48	87·89	81·93,93·86	0·09	
End	87·93	81·64,94·21		88·30	82·17,94·43		
Baseline − end	−0·22	−0·84,0·41		0·40	−0·07,0·88		0·08
BMI (kg/m²)							
Baseline	29·17	27·28,31·06	0·47	29·10	27·19,31·01	0·12	
End	29·10	27·14,31·05		29·23	27·29,31·16		
Baseline − end	−0·07	−0·28,0·13		0·13	−0·03,0·29		0·08
Total cholesterol (mmol/l)							
Baseline	6·56	6·19,6·93	0·03	6·37	5·95,6·80	0·77	
End	6·16	5·75,6·57		6·32	5·91,6·74		
Baseline − end	−0·40	−0·77,0·03		−0·05	−0·37,0·28		0·18
HDL-C (mmol/l)							
Baseline	1·09	0·98,1·21	0·16	1·09	0·97,1·21	0·77	
End	1·03	0·94,1·13		1·09	0·95,1·24		
Baseline,end	−0·06	−0·15,0·03		0·01	−0·05,0·07		0·21
LDL-C (mmol/l)							
Baseline	4·63	4·32,4·95	0·009	4·34	3·99,4·69	0·61	
End	4·24	3·84,4·64		4·23	3·72,4·75		
Baseline − end	−0·40	−0·68,0·11		−0·11	−0·54,0·32		0·22
Triacylglycerol (mmol/l)							
Baseline	1·88	1·53,2·23	0·44	1·92	1·55,2·30	0·44	
End	2·06	1·57,2·54		2·06	1·55,2·57		
Baseline − end	0·18	−0·30,0·66		0·14	−0·23,0·51		0·88

HDL-C, HDL-cholesterol; LDL-C, LDL-cholesterol.

0·74 kg body weight in the familial hypercholesterolaemic group during policosanol treatment (Table 2). This change was very small and probably not of clinical significance. It has been shown in metabolic ward studies that a change of 1 kg/m² BMI results in a small change of 0·2 mmol/l serum cholesterol (McNamara, 1994).

Supplementation with policosanol had no effect on total cholesterol, LDL-C, HDL-C or triacylglycerol in familial hypercholesterolaemic patients (Table 2). After controlling for the possible effect of lipid concentration at baseline and changes in BMI, there were still no significant differences between groups with regard to lipid concentration.

In the hypercholesterolaemic group, BMI remained constant, and policosanol supplementation resulted in significant decreases, from baseline to end, of 6% in total cholesterol and 9% in LDL-C (Table 3). However, no statistically significant differences between the changes with the placebo and policosanol treatments were shown for total cholesterol or LDL-C concentration. After controlling for the possible effect of changes in BMI and lipid concentration at baseline, the differences between the groups were still not statistically significant. No effects on HDL-C and triacylglycerol were noted.

The response in lipid variables between statin users and non-users did not differ in any of the groups. The same results were achieved when the statin users were excluded from the data analysis in the hypercholesterolaemic group (this was not done for the familial hypercholesterolaemic group because of the small number). In addition, it is clear from Fig. 1, which illustrates the individual changes in LDL-C concentration during the interventions, that the concomitant use of statins by some of the subjects did not influence the changes in LDL-C concentration compared with non-users. The total cholesterol concentrations displayed a similar response. From Fig. 1, it can also be seen that the number of subjects who showed a decrease in, increase in or lack of effect on LDL-C concentration with intake of policosanol were approximately the same as with the intake of placebo.

Discussion

The salient observation of this double-blind, randomised, placebo-controlled, crossover study was that supplementation with 20 mg/d policosanol for 12 weeks did not have any effect on serum lipid levels in a group of free-living familial hypercholesterolaemic subjects. In the hypercholesterolaemic subjects, policosanol decreased total cholesterol and LDL-C levels from baseline to end by 6 and 9%, respectively. These changes were, however, not significant when compared with placebo treatment. Policosanol treatment had no effect on HDL-C and triacylglycerol levels.

These results are in contrast to previous intervention studies that have shown highly beneficial effects of policosanol on serum lipid levels (Pons *et al.* 1994; Aneiros *et al.* 1995; Canetti *et al.* 1995; Torres *et al.* 1995; Castano *et al.* 1997; 2003*a*; 2002*c*; Crespo *et al.* 1997). Our results are, however, in agreement with those of Lin *et al.* (2004), who found that wheat germ policosanol failed to lower plasma cholesterol in subjects with normal to mildly elevated cholesterol concentrations. In recent animal studies, it has been shown that policosanol derived from rice, sunflower and sugar cane wax had no significant effects on plasma lipid levels in hamsters (Wang *et al.* 2003) or rabbits (Murphy *et al.* 2004).

The clinically effective dose range for policosanol has been determined to be 5–20 mg/d (Mas, 2000). Dosages of 5–10 mg/d were found to produce significant lipid-lowering effects (Pons *et al.* 1994; Aneiros *et al.* 1995; Canetti *et al.* 1995; Castano *et al.* 1997, 2002*c*). In this study, a daily dose of 20 mg was employed; it is therefore unlikely that the lack of a cholesterol-lowering effect was the result of too low a dose being ingested.

Although it is unlikely, the possibility that this population group might have reacted differently to policosanol supplementation from the other population groups in which significant lipid-lowering effects were reported cannot, however, be excluded.

Little is known about the mechanism of the lipid-lowering actions of policosanol. It has been suggested that policosanol has an effect on 3-hydroxy-3-methylglutaryl coenzyme A (HMG-CoA) reductase, the rate-controlling enzyme in cholesterol biosynthesis. The inhibition of enzyme upregulation by policosanol suggests that it depresses the *de novo* synthesis of HMG-CoA reductase and/or stimulates its degradation. The exact mechanism by which policosanol inhibits the activity of HMG-CoA reductase still remains unclear (Janikula, 2002; Menendez *et al.* 1994, 1997, 2001). We hypothesized that policosanol might display a lipid-lowering effect in these subjects because of its potential to inhibit HMG-CoA reductase.
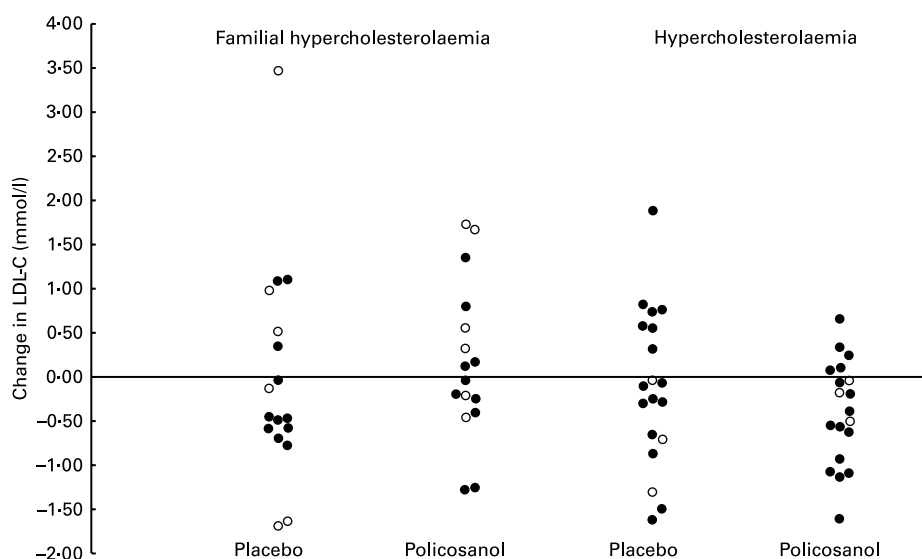

Fig. 1. Individual changes in LDL-cholesterol concentration ○, Stain users; ●, Non-stain users.

This hypothesis that policosanol operates by means of HMG-CoA reductase inhibition has, however, not yet been conclusively proven. Studies supporting this hypothesis have either been *in vitro* studies (Menendez *et al.* 1994, 2001; Lin *et al.* 2004) or animal studies (Menendez *et al.* 1996, 1997), and a recent study by Wang *et al.* (2003) has cast doubt on this hypothesis. Furthermore, it has been shown that the absorption of policosanol in the small intestine is low (Hargrove *et al.* 2004), placing some further doubt on the proposed HMG-CoA reductase mechanism.

It could be argued that the concomitant use of policosanol and statins (HMG-CoA reductase inhibitors), especially in the familial hypercholesterolaemic group, could have influenced the total cholesterol- and LDL-C-lowering ability of policosanol. To date, no studies evaluating the effects of a combined use of policosanol and statins have been published. As discussed above, the inhibitory effects of policosanol on HMG-CoA reductase *in vivo* have not yet been proved. It is clear from Fig. 1, illustrating the individual changes in LDL-C, that the concomitant use of HMG-CoA reductase inhibitors (in this case, statins) and policosanol did not confound the results.

It has also been speculated that, since the overall absorption of policosanol is low but its effects have been reported to be substantial, it could have a lipid-lowering effect at the level of the intestine (Gouni-Berthold & Berthold, 2002).

An important influential factor to consider is the composition of the mixture of higher aliphatic primary alcohols. Most of the evidence for a hypolipidaemic effect of policosanol originates from one centre (Janikula, 2002; Varady *et al.* 2003). There are, however, numerous products currently globally available that are being marketed as 'policosanol'. These products all claim measures of efficacy based on research carried out in this single centre even though their composition might be different from that of the originally patented product. Table 4 provides a summary of all the studies that have reported the composition of the policosanol supplements used, along with their effects on lipid concentrations, including the current study.

The current study, along with others (Wang *et al.* 2003; Lin *et al.* 2004) that failed to show a hypolididaemic effect, used policosanol supplements that differed slightly in composition from the policosanol supplement (Laboratorios Dalmer, Havana, Cuba) used in studies that did demonstrate lipid-lowering effects. Numerous other studies have also demonstrated lipid-lowering effects with this same supplement (Pons *et al.* 1994,1997; Aneiros *et al.* 1995; Canetti *et al.* 1995, 1997; Castano *et al.* 1995*a,b*, 1996, 1997, 1998, 1999*a,b*, 2000*a,b* 2001*a,b,c*, 2002*a,b,c,d*, 2003*a,b,c*; Batista *et al.* 1996; Benitez *et al.* 1997; Crespo *et al.* 1997, 1999; Ortensi *et al.* 1997; Mas *et al.* 1999*a*, 2001; Marcello *et al.* 2000; Fernandez *et al.* 2001; Mirkin *et al.* 2001).

A comparative study of Octa-60 from Garuda International Inc. (similar to our product) and policosanol from Dalmer Laboratories (the originally patented product) by Castano and co-workers reported significantly greater reductions in total cholesterol and LDL-C with policosanol from Dalmer compared with Octa-60 (policosanol: 20·4 % decrease in total cholesterol, 30·2 % decrease in LDL-C; Octa-60: 8·7 % decrease in total cholesterol, 10 % decrease in LDL-C; Castano *et al.* 2002*a*).

Octacosanol, which is present in the highest concentration (>60 %) in most of the higher primary aliphatic alcohol mixtures, is thought to be the active ingredient responsible for the

Table 4. Composition of different higher primary aliphatic alcohol mixtures

Reference	Policosanol source	Results	C24	C26	C27	C28	C29	C30	C32	C34
Present study	Sugar cane wax; Garuda International Inc.	Policosanol *v.* placebo ↔ TC, LDL and HDL	2·34 %	6·05 %	0·28 %	60·36 %	<0·50 %	15·21 %	4·05 %	2·37 %
Lin *et al.* (2004)	Wheat germ, Garuda International Inc.	Policosanol *v.* placebo ↔ TC, LDL & HDL	2·1 %	8·4 %	NR	67·9 %	NR	12·6 %	5·9 %	3·1 %
Castano *et al.* (2002*a*)	Sugar cane wax; Laboratorios Dalmer	Baseline *v.* end ↓TC 20·4 %, ↓LDL-C 30·2 %, ↑HDL-C 12·5 %, ↔TG	0·09 %	3·34 %	1·2 %	63·22 %	0·84 %	14·56 %	7·61 %	1·28 %
	Sugar cane wax; Blackmore's Laboratories by Garuda International Inc.	Baseline *v.* end ↓TC 8·7 %, ↓ LDL-C 10 %, ↔HDL-C, ↔TG	4·63 %	7·71 %	0·10 %	51·48 %	0·14 %	13·73 %	4·72 %	1·38 %

C24, 1-tetracosanol; C26, 1-hexacosanol; C27, 1-heptacosanol; C28, 1-octacosanol; C29, 1-nonacosanol; C30, 1-triacontanol; C32, 1-dotriacontanol; C34, 1-tetratriacontanol; TC, total cholesterol; LDL-C, LDL-cholesterol; HDL-C, HDL-cholesterol; TG, triacylglycerol; NR, not reported.

lipid-lowering actions of policosanol (Mas, 2000). However, the present study, as well as other studies using mixtures that contained sufficient amounts of octacosanol, could not demonstrate a significant lipid-lowering effect (Wang *et al.* 2003; Lin *et al.* 2004; Murphy *et al.* 2004). In light of this, it might be reasoned that the minor components in the mixture might play a more important role with regard to the lipid-lowering properties of policosanol than was previously thought. If, however, this assumption is true, the minor components must have a very powerful cholesterol-lowering effect based on the amount in 20 mg policosanol.

Conclusion

In conclusion, a dose of 20 mg/d of a mixture of higher aliphatic primary alcohols, Octa-60, displayed no beneficial effects on the serum lipid profiles of the subjects in the present study. Although there is a large body of sound clinical evidence supporting the lipid-lowering efficacy of one mixture of higher aliphatic primary alcohols, similar mixtures do not seem to display similar effects. There is a definite need to conduct comparative multicentre trials examining the lipid-lowering efficacy of all the currently produced mixtures of higher aliphatic primary alcohols.

Acknowledgements

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