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Applications of Sugarcane Wax and it's Products: A Review

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Abstract: Sugarcane wax is a product extracted from press mud, a sugar mill waste. Subsequently, D-003acids, Policosanol and Octacosanol can be derived from the extracted sugar cane wax. These compounds exhibit lipid lowering effect in animals and humans. Moreover, they are non-toxic and non-carcinogenic. The present article discusses the various applications of policosanol and presents the compilation of the studies conducted to assess the health effects of policosanol.
Keywords Sugarcane wax, Polcosanol, Octasanol, Lipid lowering

1. INTRODUCTION

Waxes in animals and plants life serve as energy stores. They are also helpful in water proofing. They contain very long chain fatty acids [1]. These fatty acids contain about 20 to 50 carbon atoms (C_{20} – C_{50}) in a molecule.

Increased Lipid peroxidation in humans is associated with aging. Sugar cane wax, a mixture of long chain aliphatic primary acids known as D-003, inhibits the Lipid peroxidation[2]. Sugar cane wax oil mainly contains palmitic, linoleic, oleic, linolenic acids, with a particular composition and ratio that are unique in sugar cane[3].

2. WAX EXTRACTION

The sugar cane wax is obtained from press mud, a solid waste from the sugar mill. A method of separation of the sugar cane wax from the press mud was explained by Phukan and Boruah [4]. The yield of hard wax varied from 3.50 to 4.10%. The colour of the microwax was light cream and it had a nominal acid value and saponification number. The degree of crystallinity (%) of the wax was 31% for the refined variety and 34% for the doubly refined variety [4]

Smith and Smith [5] compared composition of n-alkanes in the leaf waxes. The waxes contained predominantly odd alkanes C_{27} – C_{35}. The major components were in range of C_{29} and C_{31} [5].

2.1 D-003 ACID IN SUGARCANE WAX

Ledón et al. [3] studied the effects of a mixture of fatty acids from sugar cane (Saccharum officinarum L.) wax oil with two inflammation models, namely, Zymosan-induced arthritis and mice tail test of psoriasis. The fatty acid mixture exerted an important anti-inflammatory activity in both tests without evidence of irritant effects. The anti-inflammatory effect of the sugar cane by-product in experimental models of arthritis and psoriasis was then reported [3]. Gámez et. al., [6] worked on long-term carcinogenicity of D-003, in Sprague Dawley rats. When an oral dosage up to 1500mg/kg was given for 2 years, it was found to be non-toxic and non- carcinogenic. Similar study of the long-term carcinogenicity potential of D-003 sugarcane wax acids, in mice was conducted [7]. D-003 was found to be non-toxic and non- carcinogenic.

It has shown cholesterol-lowering, anti-platelet and antioxidant effects.

Lack of developmental toxicity of D-003 mixture of long-chain fatty acids in rats was also reported [8]. A major component of D-003 is 1-octacosanoic acid . It possesses effective antiplatelet, antithrombotic and cholesterol-lowering effects. D-003 was suspended in 1% acacia gum solution, and given daily by gavage to rats at dose levels of 5, 100 and 1000 mg/kg/day on days 6 through 15 of gestation. The D-003 administered up to 1000 mg/kg/day did not induce any evidence of developmental toxicity.

Rodríguez et al., [9] did the evaluation of reproductive and developmental toxicity of D-003, in rats and rabbits. The inhibition of cholesterol synthesis had a deleterious effect on reproduction. This was due to the decrease of the cholesterol and other cholesterol bio-synthesis products that were necessary for fetal development. D-003 did not induce toxic effects on reproduction. The drug-treated and control groups' offspring were comparable in growth, physical and behavioral development, spontaneous activity and reproductive performance.

Pregnant New Zealand rabbits were given D-003 as oral doses of 500 and 1000 mg/kg/day on days 6 through 18 of gestation without any evidence of embryotoxicity or teratogenicity. There was no evidence to prove that D-003 was a reproductive and developmental toxicant/teratogen.

In another study, the effect of D-003 on spinal cord injury in New Zealand rabbits were reported [10]. The increase of PgI_2 levels achieved in the D-003 treated animals was cited as an important mechanism in the protection against the spinal cord ischemia.

3. STUDIES ON POLICOSANOL

Cubeddu et al., [11] studied the comparative lipid-lowering effects of policosanol and atorvastatin. Policosanol, commonly derived from purified sugar cane wax, has been generally reported to exert lipid-lowering effects. But these researchers found that Policosanol did not reduce LDL-C or total cholesterol levels either alone or in combination with atorvastatin . Also Policosanol was safe and did not affect liver enzyme or creatinine phosphokinase levels. It was proposed that policosanol should be added to the list of nutritional supplements.

The tolerability of policosanol in the elderly population was reported [12]. The long-term tolerability of policosanol in elderly patients at high vascular risk was very good, as assessed under conditions of routine clinical practice. These results were consistent with those obtained in randomized, double-blind clinical studies of older patients treated with policosanol.

Policosanol is a mixture whose main component is octacosanol [13]. Policosanol (25, 50 and 200 mg/kg) administered by the oral route significantly reduced serum thromboxane B_2 (TXB_2) levels [13]. At 200 mg/kg it significantly increased 6-keto-$PGF_{1\alpha}$ in Mongolian gerbils. Policosanol at 200 mg/kg significantly protected against cerebral ischemia induced by unilateral ligation of common carotid artery in Mongolian gerbils. Combined administration of ineffective doses of policosanol (25 mg/kg) and aspirin (ASA) (30 mg/kg) significantly protected animals and thus indicated a synergism between them.

Alemán et al., [14] studied the effects of policosanol (50–500 mg/kg) administered orally for 18 months to male and female Swiss mice. No differences in daily clinical observations, weight gain, food consumption and mortality (survival analysis) between groups were found. There was no evidence of policosanol-induced carcinogenicity in Swiss mice.

Castaño et al., [15] compared two regimens of policosanol administered at 20mg/d for patients with type II hypercholesterolemia. The 20 mg/d dosage was particularly useful for patients at high coronary risk and to date this dosage had been administered as two 10-mg tablets once daily. The 2 policosanol 20 mg/d regimens were similarly effective. Policosanol administered as two 10-mg tablets significantly reduced total cholesterol (TC) (16.0%, $P < 0.001$ vs baseline), low-density lipoprotein cholesterol (LDL-C) (35.9%, $P < 0.001$), as well as the TC:high-density lipoprotein cholesterol (HDL-C) ratio (37.3%, $P < 0.001$) and LDL-C:HDL-C ratio (52.4%, $P < 0.001$). The differences between treatment groups were not significant. No significant changes in lipid profile variables were observed in the placebo group. The results concluded that policosanol 20 mg/d was an effective and well-tolerated cholesterol-lowering regimen whether administered as a 20-mg tablet once daily or two 10-mg tablets once daily with the evening meal.

Pons et al., [16] compared the effect of policosanol versus probucol in patients with hyper cholesterolmia. Neither policosanol nor probucol treatment significantly changed HDL-C levels. They concluded that both drugs were adequate alternatives for treating patients with type II hypercholesterolemia, with policosanol being more effective than probucol in this short-term study.

Carbajal et al., [17] studied the effects of policosanol on experimental venous and arterial thrombosis in rats. Policosanol (25 mg/kg) significantly decreased the thrombus weight, in the venous thrombosis models, the protective effect persisting until 4 hours after its oral administration. Policosanol (25 mg/kg single dose) was able to reduce rectal temperature variation induced by arterial thrombosis. Also at the same dose policosanol increased 6-keto-$PGF_{1\alpha}$ serum levels in rats.

McCarty [18] studied the effect of a combination of ezetimibe and policosanol in lowering the LDL cholesterol level in humans. LDL played a primary role in this process. The coronary risk increased as LDL cholesterol increased, throughout the entire range of concentrations encountered in healthy humans. Coronary risk was found to be minimal in individuals whose serum cholesterol remained quite low throughout life. Ezetimibe drug was cited as potent and highly specific inhibitor of an intestinal sterol permease; in daily doses as low as 10 mg, it suppressed intestinal absorption of cholesterol and decreased serum LDL cholesterol by approximately 18%. No side effects was reported in clinical doses. Its hypolipidemic activity was additive to that of statins. Both policosanol and ezetimibe was thus suggested to be administered once daily.

McCarty [19] found that Policosanol safely down-regulates HMG-CoA reductase. Policosanol lowered the cholesterol level comparable to that of statins. Moreover, it was devoid of toxic risk.

Noa and Mas [20] studied the protective effect of Policosanol on Atherosclerotic plaque on Aortas in monkeys. Policosanol had concomitant anti platelet effects. Policosanol administered on long term basis lowered the serum cholesterol and prevented the development of atherosclerotic lesions in Macaca arctoides monkeys. Mesa et al., [21] studied the toxicity of policosanol in beagle dogs for one year.

Policosanol is an entity composed of eight higher aliphatic alcohols obtained from sugar cane wax. The beagle dogs were administered policosanol for 52 weeks up to 180mg/kg/day. This dose was much higher than the maximal recommended therapeutic dose (20 mg/day) and hence indicated a good safety margin of this product. No drug related toxicity by policosanol was reported thereof.

Menéndez et al., [22] found that oral administration of policosanol inhibited in-vitro copper ion-induced rat lipoprotein peroxidation. Besides lowering the peroxidation the Policosanol also lowered the cholesterol levels. Canetti et al., [23] studied the effect of policosanol on primary hypercholesterolemia for 3 years. The long-term efficacy and tolerability of policosanol in patients with primary hypercholesterolemia was studied. The study showed that policosanol was both effective and well tolerated, which was in agreement with results of previous short- and long-term trials.

Crespo et al., [24] conducted a pilot study on the effects of policosanol on patients with non-insulin dependent diabetes mellitus and hypercholesterolemia. Policosanol was found to be effective and well tolerated in the treatment of patients with NIDDM, and hypercholesterolemia. Levels of triglyceride, glucose, and glycated hemoglobin were not significantly changed after therapy.

Castano et al., [25] studied the efficacy and tolerability of policosanol for a year in patients with high global coronary risk. After 2 months of treatment with policosanol, low-density lipoprotein cholesterol (LDL-C) and total cholesterol decreased significantly ($P < 0.00001$) by 24.7% and 15.9%, respectively. Triglycérides, which decreased significantly from 4 until 12 months, were 21.2% lower at 12 months than at baseline. Policosanol dosage of 20 mg once daily for 1 year was effective and well tolerated in patients with type II hypercholesterolemia and high global coronary risk.

Fernández et al., [26] conducted a postmarketing surveillance study on the effect of policosanol. The study population was 27,879 patients. 95.2% received 5mg/d orally and the remaining 4.8% 10-15mg/d orally. The study confirmed the tolerability of long term policosanol therapy.

Benítez et al., [27] made a comparative study of policosanol versus pravastatin in patients with type II hypercholesterolemia. Both policosanol and pravastatin were suitable alternatives for treating type II hypercholesterolemia, but policosanol administered at 10 mg/d showed modest advantages compared with pravastatin administered at the same dose.

Marcello et al., [28] conducted a pilot study on the effects of bezafibrate plus policosanol or placebo in patients with combined dyslipidemia. After 6 weeks of a standard lipid-lowering diet, 29 patients were assigned randomly to receive, under double-blind conditions, bezafibrate 400 mg/d plus policosanol 10 mg/d or bezafibrate 400 mg/d plus placebo. Treatments were taken once daily with the evening meal for 8 weeks. Coadministration

of policosanol and bezafibrate combined the benefits of both drugs on patients' lipid profiles and that the safety and tolerability of this combination was found to be very good.

Castaño et al., [29] compared the efficacy and tolerability of policosanol with lovastatin in patients with hyper cholesterolemia and concomitant coronary risk factors. The study compared the efficacy and tolerability of policosanol 10 mg/d and lovastatin 20 mg/d in patients with type II hypercholesterolemia who were at high risk for coronary events. Policosanol 10 mg/d and lovastatin 20 mg/d were similarly effective and well tolerated in treating patients with type II hypercholesterolemia and concomitant multiple coronary risk factors. Modest advantages were shown with regard to the changes in HDL-C levels and the LDL-C/HDL-C ratio.

Arruzazabala et al., [30] did a comparative study of policosanol, aspirin and their combination on platelet aggregation in healthy volunteers. The study was carried on 43 healthy volunteers for 7 days. Combined therapy significantly inhibited aggregation induced by all the agonists reaching the highest reductions of platelet aggregation induced by collagen (71.3%) and epinephrine (57.5%). Policosanol (20 mg day^{-1}) was proposed as effective as Aspirin (100 mg day^{-1}). Moreover, combination therapy showed some advantages compared with the respective monotherapies.

Ortensi et al., [31] compared the effect policosanol versus simvastatin in elderly patients with hypercholesterolemia. Fifty-three elderly patients (60 to 77 years of age) with primary hypercholesterolemia (total serum cholesterol 240 mg/dL) were enrolled. Total cholesterol, low-density lipoprotein cholesterol (LDL-C), and triglycerides were significantly reduced 14.7%, 17.9%, and 13.8%, respectively. Simvastatin significantly lowered total cholesterol 15.2%, LDL-C 19.8%, and triglycerides 8.7%. Neither policosanol nor simvastatin significantly changed high-density lipoprotein cholesterol (HDL-C) levels. Total cholesterol: HDL-C and LDL-C:HDL-C ratios were significantly lowered by both therapies. Both the drugs were concluded as adequate alternatives for treating hypercholesterolemia in elderly patients.

Carbajal et al., [32] studied the interaction of Policosanol-Warfarin on bleeding time and thrombosis in rats. Policosanol did not change the bleeding time. Warfarin alone and the combination policosanol+warfarin induced a moderate, significant prolongation of the bleeding time. The addition of policosanol to warfarin therapy did not enhance the prolongation of the bleeding time induced by warfarin alone. A significant reduction of thrombus weight was observed after policosanol or warfarin monotherapies. When the combination was used instead of either drug alone, no significant benefits were observed on the reduction of thrombus weight.

Carbajal et al., [33] studied the effect of policosanol on platelet aggregation and serum levels of arachidonic acid metabolites in healthy volunteers. Significant reductions of arachidonic acid and collagen-induced platelet aggregation were observed. Thromboxane, but not prostacyclin, generation induced by collagen was also inhibited by policosanol.

Batista et al., [34] conducted Doppler-ultrasound pilot study on the effects of long term policosanol therapy on carotid-vertebral atherosclerosis. Twenty-two patients with mild CVA, including 12 patients with type II hyperlipidemia, were enrolled. Eleven patients received 5 mg of oral policosanol twice daily. 11 patients received placebo twice daily. All the patients were treated for 1 year. Policosanol, in combination with a low-fat diet, improved hemodynamic abnormalities in patients with mild CVA and normal lipid levels or type II hyperlipidemia.

Castaño et al., [35] studied the effects of combination treatment of Policosanol and Omega-3 fatty acids on platelet aggregation.The aim of this study was to investigate the effects of combination treatment with Ω3FA (1 g/d) and policosanol(Ω3FA+Poli) compared with Ω3FA (1 g/d) plus placebo (Ω3FA+Pla) on platelet aggregation in human patients with hypercholesterolemia. Policosanol (10 mg/d) administered concomitantly with Ω3FA (1 g/d) enhanced the inhibition of platelet aggregation to AA and collagen, but not to epinephrine.

Zardoya et al., [36] studied the effects of Policosanol on the hyper cholesterolemic patients with abnormal serum biochemical indicators of hepatic function. Policosanol was found to be effective and well tolerated in patients with type II hypercholesterolemia and abnormal serum biochemical indicators of hepatic function.

Pons et al., [37] studied the efficacy and safety of Policosanol in patients with primary hyper cholesterolemia and found the policosanol therapy was effective and very well tolerated.

Echenique et al., [38] worked to find the effects of Policosanol chronically administered in male monkeys (Macaca arctoides). 18 adult male *Macaca arctoides* monkeys were used to study the cholesterol-

lowering effects and possible toxicity produced by oral administration of policosanol (0.25, 2.5 and 25 mg/kg) for 54 weeks. After 8 weeks, a significant reduction of serum total cholesterol and low-density lipoprotein cholesterol was observed in policosanol-treated animals when compared with the controls.

Policosanol (0.25–25 mg/kg) administered orally for 54 weeks brought about a persistent reduction in blood cholesterol levels and was very safe and well tolerated during long-term administration.

Aneiros et al., [39] studied the effect of successive dose increases of policosanol on the lipid profile. They also studied the tolerability of the treatment. Effects of successive dose increases of policosanol on the lipid profile and tolerability of treatment was investigated on 33 patients. The greater reductions in LDL-C, total cholesterol, and atherogenic ratios at the end of week 12 indicate the effectiveness of a successive dose increase regimen. Policosanol was again found to be well tolerated.

Berthold and Berthold [40] studied the clinical pharmacology and the therapeutic significance of Policosanol. They found Policosanol as a very promising phytochemical alternative to classic lipid-lowering agents such as the statins.

Jones et al., [41] claimed that according to some independent researchers Policosanol was not an effective agent for LDL-cholesterol (LDL-C) lowering in humans. It was also reported by Berthold et al. [42] that Policosanol does not lower cholesterol in Caucasian patients.

Más et al., [43] studied the effects of Policosanol on postmenopausal women with type II hypercholesterolmia. Taylor et al., [44] studied the effect of Octacosanol on human health. They found it to have lipid lowering effect and anti aggregatory properties. Guardamagna et al., [45] treated hyper cholesterolemic children with red yeast rice extract and Policosanol. They studied the efficacy and safety of the treatment. The treatment with a dietary supplement containing red yeast rice extract and policosanols was for the first time successfully employed in hypercholesterolemic children. The strategy was found effective, safe and well tolerated in a short-term trial.

Due to the growing realization of the applications of Policosanol and the Octacosanol new methods have also been investigated for their extraction from their sources, the Sugar cane wax and the Press Mud or the Filter mud from the sugarcane juice clarification. A solvent-free extraction process for Policosanol was reported recently [46].

Ou et al., [47] prepared Octacosanol from the press mud produced after sugar cane juice clarification. Filter mud from sugarcane juice clarification contained 6.85 g/100 g waxes per 100g of dry mud. It was used for octacosanol extraction. Saponification of the waxes extracted by hot ethanol reflux extraction has significantly increased octacosanol content to 47.8 g/100 g, per 100g of sugar cane wax.

4. CONCLUSION

The sugar cane wax derived from the press mud waste has a variety of significant applications. More investigative work may bring out new applications.

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