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Review Article

Exploring the Pharmacological Benefits of Policosanol in Herbal Medicine

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ABSTRACT

Policosanol is a mixture of high molecular weight primary alcohols with Long-chain length of 24 to 34 carbon atoms. It was originally isolated from sugarcane (Saccharum officinarum L.) wax. Natural mixture of long chain alcohols includes tetratriacontanol, triacontanol, octacosanol, hexacosanol and tetracosanol. Policosanol is one of several natural products that have been studied as potential effects in various disease treatments. Policosanol has been used as a lipid-lowering agent, drugs for ischemic stroke, dyslipidemia as an antiplatelet aggregation, antioxidant effect, treatment of arteriosclerosis, agent to prevent cardiovascular risk, enhancement of neurological function in patients with neurodegenerative diseases such as Alzheimer disease, Parkinsonism disease, brain stroke etc. In this study explore the potential benefits of Policosanol in the management of various diseases. However, the bioavailability of policosanol remains a subject of debate, with variations observed based on formulation and study design. This review aims to provide a comprehensive overview of policosanol's chemistry, mechanisms, pharmacological uses, bioavailability, and safety, highlighting its potential as a natural therapeutic agent, including extraction procedures with addition; it will help to develop medicinally useful drugs and functional foods in the future.

INTRODUCTION

Policosanol is an aggregate of excessive molecular weight aliphatic primary alcohols with long-chain length of 24 to 34 carbon atoms. Herbal mixture of long chain alcohols includes tetratriacontanol, dotriacontanol, triacontanol, nonacosanol, octacosanol, heptacosanol, hexacosanol and tetracosanol. These compounds are rather insoluble substances in aqueous media at room temperature and are white powder or crystal solid and hard, characterized by means of their non-

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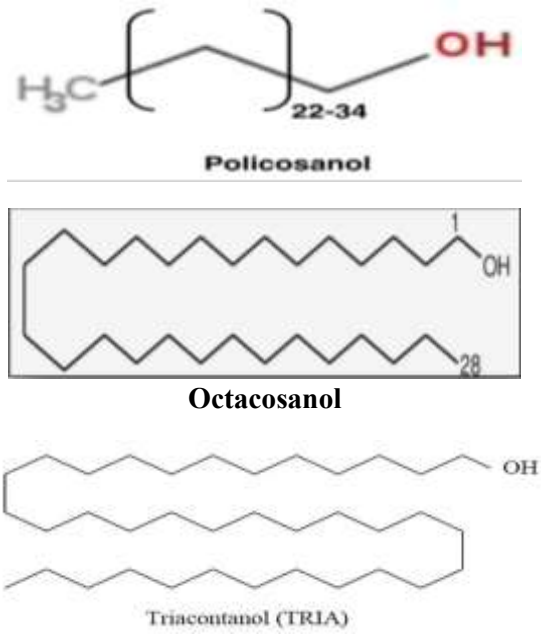
polar nature and really high boiling factors. Numerous useful residences had been said, both to human health and as an increase promoter in plant life and cyanobacteria.[1] It is extracted from rice bran, sugar cane, germ, maize, beeswax, apples, grapes, and many others. Policosanol also are located in the leaves, end result, nuts, and a seed of many foods. Policosanol became in the beginning isolated from sugarcane (Saccharum officinarum L.) wax.[2] Policosanol is one in all several natural products that have been studied as potential effects in diverse ailment remedies. Policosanol has been used as a lipid-lowering herbal drug inside the alternative medicine and ancillary drugs for heart diseases, dyslipidemia,[3] as an antiplatelet aggregation, antioxidant effect, remedy of arteriosclerosis, agent to save you cardiovascular risk,[4] enhancement of neurological feature in sufferers with neurodegenerative illnesses inclusive of Alzheimer sickness, parkinsonism sickness, mind stroke etc. Policosanol from milk thistle oil well-known shows a potential anti-arthritic, as a result may be used for the treatment of sicknesses like rheumatoid arthritis[5] while which has additionally been proven to reduce serum uric acid levels and as such may be very useful in the management of patients with gout.[6]

Chemistry of Policosanol:

Policosanol exists in nature as a white crystal or powder that consists of a mixture of alcohol esters with carbon chains starting from 22 to 34 in period. Those alcohols include docosanol (C-22), tetracosanol (C-24), hexacosanol (C-26), octacosanol (C-28), nonacosanol (C-29), triacontanol (C-30), dotriacontanol (C-32), and tetratriacontanol (C-34), which might be most effective stable in nature as a mixture (Policosanol).[3] most customary aliphatic alcohols in Policosanol are octacosanol, hexacosanol and triacontanol. The pleasant of this natural product relies upon on its source and composition.[5] even as essential components of herbal computers are octacosanol (C28), (60 – 70%)triacontanol(C30),(10–15%) and hexacosanol (C26)(four.5 – 10%).[6,7] Policosanol is a herbal combination of aliphatic number one alcohols which are remoted from purified sugar cane *(Saccharum officinarum L)* wax by means of hydrolytic cleavage and next purification. The chemical method is CH3— (CH2) n—CH2OH with chain period varying from 24 to 34carbons atom.[8]

Chemical structure of policosanol,[9] octacosanol,[10] triacontanol[11] in fig. no. 1



Mechanism of action of policosanol:

Policosanol appears to purpose reduced synthesis and multiplied degradation of three-hydroxy-three- methylglutaryl Coenzyme A (HMG-CoA), the price-proscribing step in LDL cholesterol synthesis. This is special than the mechanism of action of statin tablets, which paintings by using competitively inhibiting HMG-CoA reductase enzyme.[12] The proposed mechanisms of action of Policosanol are multiple, it binds to the β-subunit of adenosine 5′-monophosphate (AMP)-activated

protein kinase and turns on the AMPK pathway which suppresses the interest of three hydroxy-3-methyl glutaryl coenzyme A (HMG-coA) reductase enzyme which ends to an expanded receptor-mediated uptake of LDL within the liver thru growing hepatic LDL receptors.[13] In addition, AMPK activation results in the inhibition of cholesteryl ester switch protein (CETP), therefore stopping the binding of HDL and LDL to CETP with resultant growth in LDL catabolism and a decrease inside the metabolism of triglycerides (TGs). Inhibition of CETP activity can also result in anti-inflammation and anti-growing old consequences ensuing in tissue regeneration and cellular replication.[14] Through AMPK activation, Policosanol may also suppress the hobby of sterol regulatory detail-binding protein-2 (SREBP2) by using inhibiting its nuclear translocation leading to reduced LDL cholesterol biosynthesis.[15]

Policosanol inhibits the phosphorylation of p38 mitogen-activated protein kinase (p38MAPK), thus suppressing the results of the p38MAPK pathway. There are four p38MAPKs namely p38α (expressed in maximum cell types), p38β (expressed in the mind), p38γ (expressed in skeletal muscle), and p38(expressed in endocrine glands), inhibition of those kinases suppresses the p38MAPK pathway, leading to at once reduced expression of apoptotic and atherosclerotic genes.[16] Policosanol enhances the boom of human dermal and mind glial cells thru p38α and p38β MAPK based inhibition of apoptosis. That is related to elevated cell variety and reduced manufacturing of reactive oxygen species. Policosanol additionally reduces the buildup of fats in hepatic tissue. Policosanol can also suppress1-methyl-4-phenyl-1,2,3,6-tetrahydropyridine (MPTP) which induces the phosphorylation of c-Jun-N-terminal kinase (JNK) that has been implicated in Parkinsonism. Moreover, the ProNGF and NGF signaling pathways also are inspired by Policosanol as a part of its anti-Parkinson outcomes.[17]

Extraction of policosanol:

long-chain (C22–C34) aliphatic primary alcohols which are derived from sugarcane and are known as policosanol, more than 30 years in the past, a research crew in Cuba separated and purified policosanol from sugarcane *(Saccharum officinarum L.)* wax.[21] (Given in figure no.2) Latter researchers determined that it is able to additionally be extracted from different foods, which includes wheat germ, beeswax and rice.[18] Policosanol additionally existed within the leaves, fruits, nuts and seeds of many flora, however the commercially extracted from sugarcane wax.[19] Sugarcane policosanol turned into a mixture of aliphatic alcohols with additives that encompass tetratriacontanol, dotriacontanol, triacontanol, nonacosanol, octacosanol, heptacosanol, hexacosanol and tetracosanol. Amongst them, octacosanol was the most considerable and considered to be the number one lipid-lowering additives, lessen platelet aggregation as well as save you atherosclerosis development. In 1991, sugarcane policosanol became authorized as a lipid-lowering agent in Cuba, and since then, it has been bought as a business tablet in many countries together with the United States, Canada and Caribbean regions.[20]

Fig. No. 2 White Crystalline Powder of Policosanol from Sugarcane (Saccharum Officinarum L)

Extraction Techniques of Policosanol:

Saponification:

Saponification is utilized in fats extraction, and technique is suitable for policosanol extraction.[22] dry saponification yielded the finest amount of octacosanol and triacontanol amongst four extraordinary strategies of extraction, and the yield: dry saponification> saponification with alcohol > saponification with water > trans-esterification. To isolate policosanol through saponification petroleum ether used as a solvent. High-overall performance skinny-layer chromatography (HPTLC) became used to assess the content of policosanol.[23]

Solvent extraction:

Solvent extraction is a traditional and powerful approach, in which organic solvents such as ethanol or hexane used to extract policosanol. Jung and his colleagues[24] used roasted perilla seeds and natural solvent to extract policosanol. The policosanol extract changed into recognized by using GC–MS/MS analysis and the yield of policosanol become 302.forty mg/kg. Giuffre and Capocasale hired Soxhlet-petroleum ether to extract policosanol from tomato seeds at a boiling factor of 40–60 °C. They observed that the composition of three tomato cultivars are find out Seven long-chain fatty alcohols are found within the tomato seed extract, and they may be docosanol (C-22), tricosanol (C-23), tetracosanol (C-24), pentacosanol (C-25), hexacosanol (C-26), heptacosanol (C-27) and octacosanol (C-28). Octacosanol is the highest content material compound and the content is from 39.22% to 41%.[25]

Trans-esterification and molecular distillation:

Trans-esterification method normally used for separation of octacosanol. song and his colleagues used trans-esterification to extract policosanol from sugarcane wax, the yield of the most ample aliphatic alcohol is 17.34%[26] Butanol became also used to extract octacosanol from rice bran wax and response floor methodology turned into used to optimize the yield of octacosanol become 53% The foremost composition of molecular distillation turned into determined to be triacontanol. The octacosanol content in distillates is multiplied to 37.6% at a 105 °C and it is 48% greater than the trans-esterification study.[27]

Ultrasonic-assisted extraction:

Excessive-intensity ultrasound extraction method makes use of sound waves to agitate the solvent and is pronounced to isolate octacosanol from distinctive uncooked substances. Cravotto and his colleagues recommend that ultrasound at 18.2 kHz, three hundred W, 45 °C for 30 min the usage of to extract octacosanol from rice bran is greater effective than the use of Soxhlet extraction method.[28] in comparison with the trans-esterification approach, the time of ultrasound extract era is shortened and the octacosanol yield is extended.[29]

Microwave-assisted extraction:

It becomes first used by Venturelli and his team for Policosanol extraction. This technique isn't always possible on a huge scale because of its high manufacturing cost, it reduces pattern education time and increases product yield.[30]

Pharmacological Uses of Policosanol:

Policosanol has several useful physiological effects in the field of medication which include its use as an organo-gel for neutraceutical and drug shipping purposes[31] as platelet anti- aggregation, an agent to relieve intermittent claudication and to save you different cardiovascular dangers. Different properties of Policosanol include lipid-

lowering.[32] It has also been shown to prevent and alleviate signs and symptoms related to neurodegenerative issues, which includes Alzheimer's sickness and Parkinson's disease.[33] Policosanol canreduce endothelial damage, and foam mobile formation[34] increasing muscle endurance[35] enhancing overall performance of coronary heart disease sufferers for the duration of exercise[36] in addition, policosanol promotes skin wound healing in mice; exhibits antibacterial, anti-inflammatory, and analgesic properties; and is skin-secure[37] Furthermore, it has been suggested to motive proliferation of human follicle dermal papilla cells[38] and promote hair growth in androgen-brought on alopecia mice[39] Octacosanol has been proven to have anti-inflammatory effects outcomes whilst triacontanol can save you oxidative stress, set off induce anti-inflammatory responses and inhibit lipid peroxidation. Then again, hexacosanol has been established a capability to reduce hepatic and plasma LDL cholesterol via the AMPK pathway and suppression of SREBP2 in HepG2 and C57BL/6J mice associated with diabetic headaches and neurodegenerative.[40] In recent studies, it turned into suggested that octacosanol, of policosanol has antibiotic homes and impacts energy metabolism.[41] It also inhibits dextran sulfate sodium (DSS) caused colitis.[42]

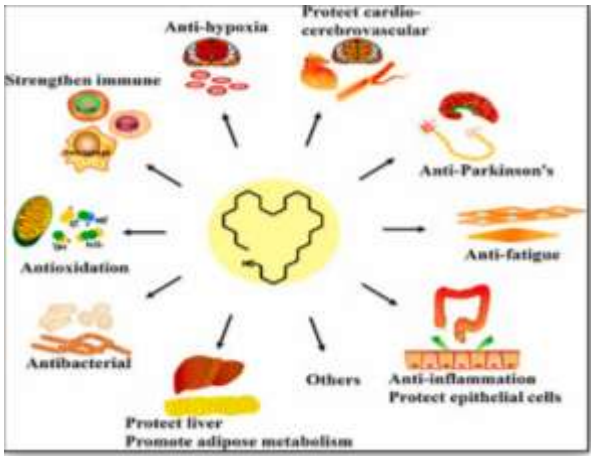


Fig. no. 3 Numerous Pharmacological Uses of Policosanol[43]

Policosanol in hypercholesterolemia:

Cholesterol is needed to preserve membranes and bring steroid hormones, vitamin D, and bile acid. however, abnormally improved levels of cholesterol within the blood, specially low-density lipoprotein (LDL) cholesterol, called hypercholesterolemia.[44] Intracellular levels of cholesterol are tightly managed by cholesterol secretion into blood and activation of b-hydroxy-methylglutaryl-CoA(three-hydroxy-3-methylglutaryl-CoA[HMG-CoA]) reductase.[45] When cholesterol levels are high within the cells, AMPK phosphorylation deactivates phosphorylation of HMG-CoA reductase.[46] therefore, HMG-CoA reductase inhibitors, called statins, which include atorvastatin, lovastatin, and simvastatin, had been correctly used for lowering LDL cholesterol. However, long-term intake of those drugs may cause side effects which include muscle pain and harm, liver damage, diabetes, and neurological side consequences. Consequently, there is growing interest in the potential of medicinal plants that exhibit hypo-cholesterolemic impact.[47]

Policosanol is considered one of numerous "natural" products that have been studied as capability lipid-decreasing retailers. policosanol has been shown to lower general cholesterol (TC) through 15% to 25% and occasional-density lipoprotein cholesterol (LDL-C) by way of 20% to30%, and to elevate high-density lipoprotein LDL cholesterol (HDL-C) with the aid of 5% to 15%.[48] Acetate and mevalonate are two biochemical intermediates located in the endogenous LDL cholesterol biosynthesis pathway. Acetate is converted to mevalonate by means of 3-hydroxy- 3-methyl-glutaryl CoA (HMG-CoA) reductase enzyme[49] policosanol reduce synthesis of HMG-CoA reductase or enhance its degradation at dose degree 5mg-20mg/day and hence slowing endogenous

cholesterol biosynthesis prior to the production of mevalonate.[50]

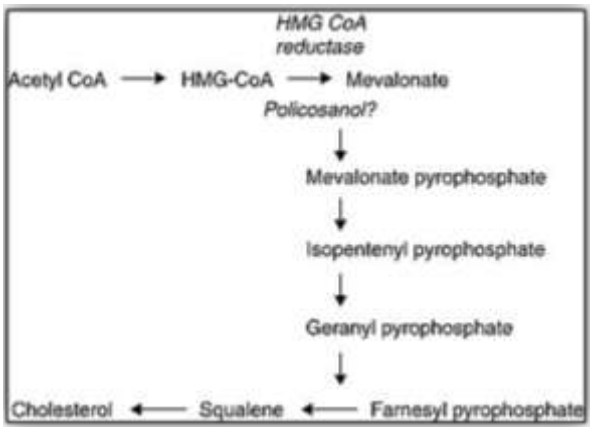


Fig. no. 4 Action of Policosanol on HMG-COA Reductase Enzyme[51]

Policosanol in neurodegenerative illnesses:

Alzheimer Disease:

One of the neuro-pathological features of Alzheimer's ailment (AD)may be the accumulation of neuronal plaques referred to as beta-amyloid (Aβ) plaques and neuro-fibril coils resulting from the accumulation of microtubule-established protein hyper-phosphorylation, which includes intracellular Tau protein.[52] The activation of glial cells released the advert-associated cytokines such as IL-1β, IL-6, and TNF-α, in addition to ROS era. As a result, the unusual and anti-inflammatory immune response extended free radicals or reduced antioxidant defense mechanisms are associated with neuronal cell death and harm. Oxidative stress is an essential pathogenic issue happening inside the early level of AD.[53]

Currently, confined wide variety of medicine is effective against advert, and just a few drugs, such as acetyl cholinesterase inhibitors and N-methyl-D-aspartate receptor antagonists, were approved through the U.S. food and Drug management for the treatment of advert. These pills offer short term relief to adverse sufferers with mild to moderate signs and feature apparent side results. For this reason, efforts have been made to broaden strategies that target Aβ for the prevention and treatment of AD. It's miles particularly essential to explore herbal sources for drugs with fewer facet results and high efficacy.[54] According to traditional chinese remedy, white wax is mainly composed of policosanol, hexacosanol, and octacosanol. Policosanol has been proven to reduce lipid levels in blood and alleviate the signs related to diabetic complications and neurodegenerative disorders, such as Parkinson's sickness and advert. In ad policosanol lower the AB plaque formation and hyper-phosphorylation of intracellular Tau protein, because of its antioxidant, anti-glycation, anti-inflammatory and hypolipidemic effects. For remedy of Alzheimer's sickness. Management of policosanol turned into completed at 50 mg/kg body weight.[55] Policosanol decreased the Aβ-prompted toxicity by using up regulating the expression of genes associated with heat surprise reaction and oxidative strain, and down regulating the expression of bcat-1, that's concerned inside the glutamine cysteine synthatase pathway and have to be explored similarly as a drug target in advert.[33]

Parkinson Disease:

Parkinson's ailment (PD) is a progressive and age-related neurodegenerative disease characterized by way of degeneration of dopaminergic neurons originating in the substantia nigra pars compacta and projecting to the dorsal striatum.[56] To date, the maximum broadly used and powerful treatment for PD is presently available dopamine replacement techniques through oral supplementation of dopamine (DA) precursor levodopa, however, long-term treatment with levodopa is regularly complex by way of the development of unfavorable results.[57] There were additional anti-Parkinson pills, which includes

dopamine receptor agonists, however those available healing procedures could not shield in opposition to dopaminergic neuro-degeneration. Therefore, it is most important to increase new pills that show or halt the rate of progression of PD.

Octacosanol appreciably inhibited the elevated expression of the 6-OHDA-brought about proNGF-p75NTR-sortilin demise signaling complicated and consequently its downstream effector proteins. Studies found out that proNGF that's a precursor of NGF can act with aco-receptor of p75NTR and sortilin to alter. In the meantime, NGF triggered neuronal survival via TrkA and p75NTR with low-affinity binding.[58] As a result, p75NTR appeared as a molecular signal with which could mediated each cell survival and mobile demise. On one hand, administration of octacosanol at a dose of 70 mg/kg strongly blocked the 6-OHDA-induced growth in proNGF. However, administration of octacosanol at a dose of 35–70 mg/kg significantly suppressed the 6-OHDA-inspired up-regulation of p75NTR and sortilin. Octacosanol become proven to ameliorate neurotoxicity in 1-methyl-4-phenyl-1,2,3,6 tetra-hydropyridine (MPTP)- dealt with C57BL/6N mice. Thinking about its extremely good tolerability, octacosanol is probably taken into consideration as an agent for clinical application in treating Parkinson's sickness.[59]

Brain stroke and atherosclerosis:

Ischemic stroke is a cerebrovascular ailment that happens as a trouble of atherosclerosis and consists of a surprising neurological deficit because of problems in cerebral blood circulate.[60] The release or activation of unfastened radicals, as well as eicosanoids, infection, immune response, and lipid degradation products, are worried in its pathogenesis, which act after primary ischemic damage, either sequentially or in parallel, to reason cellular death. Several pharmacological agents may be used for each opportunity, with thrombolytic remedy and antiplatelet drugs being broadly used for the intense phase and for stroke restoration and prevention, in addition to neuro-protectants and antioxidants respectively.[61] Antiplatelet pills, LDL cholesterol-lowering capsules, such as the inhibitors of 3-hydroxy-3-methylglutaryl-Coenzyme A (HMG-CoA) reductase (statins), are beneficial in the intense segment, but also for prevention of stroke in secondary prevention sufferers. Widely, pharmacological treatment plans used inside the stroke prevention have not finished scientific efficacy relevant, to the time they present unfavorable outcomes that restrict their intake. Consequently, the development of recent substances to save you or deal with ischemic stroke is needed.

Policosanol has lipid-decreasing, antiplatelet, antioxidant and vascular endothelium defensive residences, all of which give it a complete anti-atherosclerotic effect.[59] policosanol has outstanding pleiotropic outcomes useful for managing atherothrombotic diseases, such as the inhibition of platelet aggregation and the inhibition of the susceptibility of LDL to undergo lipid peroxidation.[62] For treatment of Atherosclerosis policosanol administered at dose stage 10mg/ day. Decrease on LDL-C tiers is a cause strong enough to support protective vascular consequences; a number of these effects of policosanol may be finished through mechanisms other than lipid reducing, which include its antiplatelet and antioxidant consequences. Taken together, these observations suggest that treatment with policosanol, characterized by means of cholesterol-decreasing and relevant pleiotropic effects could reduce stroke hazard and enhance clinical evolution and final results as soon as a stroke has befell. Cuban policosanol became secure and well tolerated, and not using a serious

adverse activities going on in the course of the trials. Consequently, the clinical evidences showed the protective and anti-stroke results of Cuban policosanol.[63]

Policosanol in platelet aggregation:

Platelets play a critical function in each thrombosis and atherogenesis and the rationale for the usage of antiplatelet tablets inpatients with excessive atherosclerotic chance has been demonstrated, their use being encouraged for all sufferers with established atherosclerotic ailment.[64] Policosanol decreases platelet aggregation by means of decreasing the synthesis of platelet-aggregating thromboxane B2 (TXB2), antithrombotic assets because it inhibits the formation of thromboxane A2 (TXA2) without an impact on prostacyclin (PGI2). Policosanol reduces platelet aggregation triggered by means of a number of experimental materials, with dose-established increases from 10-50 mg/day. Policosanol by myself at 20 mg/day was more effective than a hundred mg aspirin at lowering platelet aggregation prompted through ADP, and similarly effective when induced by means of epinephrine and collagen.[65] despite reduced platelet aggregation, there has been no increase in coagulation time when policosanol became taken by myself; but, while mixed with one hundred mg/day aspirin, coagulation time increased.

Policosanol in weight problems:

Weight problems effects from a persistent imbalance among strength/carbohydrate consumption and expenditure. Obesity is a strong danger aspect for metabolic sicknesses which includes type 2 diabetes mellitus, atherosclerosis, hyperlipidemia, and non-alcoholic fatty liver ailment.[17] Policosanol can boom the electricity expenditure of adipose tissue, thus status as a promising healing target for the control and alleviate diet-triggered weight problems and weight problems- associated metabolic problems via improving hepatic lipid metabolism and growing brown adipose tissue interest. Further, confirmed that the consumption of policosanol derived from barley sprout extracts substantially reduces the burden of the experimental animals.[66]

Policosanol in hypertension:

Hypertension is report of a systolic blood strain ≥ a hundred and forty mmHg or a diastolic blood pressure ≥ ninety mmHg on one-of-a-kind days. In a scientific evaluate and meta-evaluation, it changed into proven that Policosanol appreciably decreases each systolic and diastolic blood strain[67] extended intake of Policosanol significantly reduces peripheral blood stress in addition to aortic blood pressure in wholesome Korean subjects in a dose-dependent way further, quick-term intake of Policosanol appreciably reduces both systolic and diastolic peripheral blood pressure in addition to systolic and diastolic aortic blood strain and mean arterial strain in healthful Korean topics with pre-high blood pressure in a dose-structured way. Policosanol became discovered to significantly reduce the common systolic blood stress level through 10% and the common diastolic blood stress level by using 14% in healthful ladies.[68] Policosanol reduces both systolic and diastolic blood pressure in type II diabetic patients with dyslipidemia. Policosanol have accurate antihypertensive properties; extensively decreasing both systolic and diastolic blood stress in many clinical trials from Cuba and different parts of the arena.

Policosanol in diabetes:

Diabetes is a persistent metabolic ailment that is characterized by way of high blood glucose because of either an in potential of the pancreas to supply sufficient insulin or the frame's incapacity

to effectively make use of the insulin produced. Numerous researches have confirmed the anti-diabetic consequences of Policosanol. For treatment of DM dose of policosanol administered 20-40mgday orally. The hypoglycemic effect of Policosanol has particularly been attributed to signaling pathways which increase glucose uptake by means of the skeletal muscle and inhibit hepatic gluconeogenesis.[17] Several outcomes of Policosanol on glucose metabolism were pronounced in each human and animal study. At basal glucose stage, Policosanol causes a 5% boom in insulin secretion even as at excessive blood glucose stages it cause a 14% boom in insulin secretion. Policosanol have a hypoglycemic impact that's greater pronounced compared to different dyslipidemia pills (e.g. Atorvastatin) or herbal merchandise (e.g. omega-three fatty acids).[69] Similarly, Policosanol enhances the metabolism of nutritional fat and glucose main to ideal reduction of blood glucose and levels of cholesterol. Policosanol may want to reduce fasting glucose degree, and enhance tissue insulin sensitivity. Policosanol ought to appreciably lessen the level of glucose in a test on Zebra fish. Conclusively on Policosanol in diabetes, it has been shown Policosanol possesses anti-diabetic impact each in human and animal experiments.

Policosanol in cardiovascular and cerebrovascular diseases:

It has been pronounced that a food regimen of policosanol with crimson yeast rice, berberine, folic acid, coenzyme Q10 can reduce lipid concentration in statin-illiberal patients.[70] Policosanol has anti-ischemic outcomes and is used to treatment cerebral vascular disorders in cerebral-ischemia induced Mongolian gerbils, therefore it could represent a dietary supplement for the remedy of cerebrovascular disorders. Policosanol was proven to ameliorate myocardial necrosis in an isoprenaline-triggered myocardial necrosis mouse version. One study found that treatment with policosanol drastically reduced the size of infarctions, with numbers of polymorpho-nuclear and mast cells reducing in isoprenaline-stimulated myocardial necrotic mice.[71] Policosanol averted damage to endothelium in rabbits and reduced intimal thickness in arterial walls. The administration of policosanol in animals reduced the chance of atheroma resulting in decreased platelet aggregation, foam cell formation and endothelial damage. Octacosanol increased proliferation and migration of HUVECs and regulated these effects via activation of the PI3K/Akt and MAPK/Erk1/2 signaling pathways. Octacosanol is a capability anti-hypercholesterolemic agent for sufferers with low chance of cardiovascular disease.[72]

Policosanol in ulcer and most cancers:

Isolates from bee wax, which include 26.63% triacontanol, 17.49% octacosanol and other primary better alcohols can surely save you the prevalence of acute gastric ulcers because of water-immersion pressure in mice.[73] octacosanol from the leaves of S. grisea had anti-nociceptive and anti-inflammatory consequences, probably are related to the pharmacological manipulate of pain and anti-inflammatory tactics. octacosanol now not only inhibits the proliferation of Ehrlich ascites tumor cells however also can inhibit the secretion of ascites fluid in proliferating tumor cells in vivo. Policosanol containing 7.64% octacosanol was shown to reduce irritation in murine peritoneal macrophages and notably reduced secretion of IL-1β and TNFα. A recent have a look at showed that octacosanol ameliorated gut inflammation each in vitro and in vivo.[74] Octacosanol extensively blocked the expressions of TNFα, IL-6, IL-1β and iNOS each in vitro and in vivo and down regulated the expressions of p-p38 and p-JNK.

Policosanol in sleep development and exhaustion:

Octacosanol possesses strain discount and sleep-improving residences.[75] management of one hundred and 200 mg/kg octacosanol resulted in a large boom in non-speedy eye motion (NREM) sleep in comparison to that of car and decreased sleep latency. Oral management of octacosanol in workout-educated rats appreciably superior creatine phosphokinase hobby in plasma and citrate synthase pastime in muscle. Supplementation with octacosanol within the food plan of exercise trained rats reduced muscle glycogen storage and expanded muscle oxidative capacity.

Policosanol as an Antioxidant:

Policosanol possesses mighty antioxidant belongings with the aid of reducing the formation of reactive oxygen species (ROS) via decreased nicotinamide adenine dinucleotide phosphate (NADPH) oxidase inhibition and stimulation of the sports of catalase and superoxide dismutase.[76] Octacosanol lipophilicity and its large shape reduced extended solubility in water ensuing in poor absorption and a low bioavailability. Sodium salt of octacosyl sulfate changed its solubility; and modified octacosanol displayed maximum lipid peroxidation activitiesat a concentration one thousand ppm.[77]

Policosanol as an Antimicrobial agent:

Octacosanol remoted from P. aurantiacum tested antibacterialinterest, particularly almost about S. flexneri, k. pneumonia and S. typhi. Furthermore, it also showed anti-dermatophytic interest particularlytowards T. ajelloi.[78] Octacosanol extracted from rice bran demonstrated comparableantibiotic activity in comparison with the routinely-used antibiotictiamulin.

Energy-metabolism promoting effect of policosanol:

Octacosanol can sell the phosphorylation of AMPK, enhancing the generation of ATP and suppressing cholesterol synthesis in cultured rat hepatic most cancers cells. Furthermore, outcomes from a specific observe indicated that octacosanol can enhance the secretion of T3, GH, GU and advert in the blood of weaning piglets and up regulate the expression of genes related to blood hormones in liver and muscle mass, therefore enhancing growth performance and decreasing the strain response.[41]

Policosanol in irritation:

Irritation is a physiological reaction precipitated by way of infections or tissue harm or can be a feature of some sicknesses, and plenty of studies have proven that policosanol or its compounds show anti-inflammatory activity. Policosanol purified from beeswax, decreased oedema formation and inhibited Myeloperoxidase (MPO) interest. MPOs are peroxidase enzymes produced through neutrophils that generate reactive oxidants, contributing to their microbial pastime. These results advise that the anti-inflammatory effect of policosanol may be due to inhibition of MPO thru the discount of neutrophil infiltration into broken tissue. tetracosanol, hexacosanol and octacosanol inhibits the generation of nitrite, Prostaglandin E2 (PGE2) and TNF-α respectively.it has been said that policosanol inhibits Nitric Oxide Synthetase(iNOS) protein and controls the high manufacturing of Nitric Oxide (NO) in the course of infection by inactivating NF-κB via mechanisms along with the ones used by statins. Therefore, this effect may be associated with the hypothesis that policosanol inactivates or blocks the nuclear translocation of NF-κB, even though the molecular mechanisms have not yet been elucidated. octacosanol

decreases nuclear ranges of p65 and c-Jun, which are components of the transcription elements NF-κB and AP-1. octacosanol also inhibits the pastime of NF-κB and AP-1 and the phosphorylation of p38 and JNK, reducing the expression of pro-anti-inflammatory cytokines and main to a reduction in the anti-inflammatory procedure. On the give up end is policosanol, octacosanol and traicontanol inhibit nuclear translocation of NF-κB and the phosphorylation of MAPKs, thereby lowering the expression of the anti-inflammatory mediators. Alternatively, policosanol additionally inhibits vascular permeability, oedema, and interest of the MPO peroxidase enzyme, decreasing the manufacturing of reactive oxidants by way of neutrophils.[79]

Bioavailability of policosanol:

Bioavailability is an important component because of affecting the ultimate effectiveness of useful foods. The bioavailability of Policosanol is less than 10% while taken orally, however has a tendency to be advanced both by using nano-emulsification or through esterification with oleic acid.[80] To beautify the bioavailability of policosanol, a change of policosanol for a nano-emulsion method became done. Policosanol is a water-insoluble substance and it became prepared through oral suspension with the use of acacia gum, that's a solvent of policosanol.[68] Policosanol is metabolized via the liver and excreted via the kidney. It orally administered, reaching height degrees from 30 to one hundred twenty minutes after ingestion in extraordinary animal species and humans. After absorption there's a liver first-skip effect. Radioactivity research reveals fundamental distribution into the liver, with a lot smaller uptake noted inside the coronary heart, aorta, fats, and plasma. Excretion is typically fecal.[2]

Safety profile of policosanol:

All protected research confirmed that policosanol tested no damaging consequences on liver and renal feature signs. An excluded look at additionally suggested that sugarcane policosanol was efficacious and nicely tolerated in patients with hypercholesterolemia coupled with improved biochemical parameters of hepatic feature. The detrimental reactions in policosanol organization participants included symptoms acidity, constipation, nausea, diarrhea, polyphagia, headache, dizziness, anxiety, polydipsia, skin dryness. Maximum adverse outcomes have been brief, mild and unusual.[81] The protection profile of Policosanol has been nicely installed. Policosanol is secure each in animal and human fashions with first-rate health benefits. When Policosanol is utilized in mixture with the statins e.g. atorvastatin, simvastatin, or other lipid-lowering dealers, it enables to attenuate or neutralize the toxic impact of those dealers. Policosanol is broadly speaking secure whilst taken among doses of 5 mg to 80 mg orally for duration of up to three years. Numerous literatures have said that Policosanol suggests secure and very useful in the control of metabolic hazard elements or metabolic syndrome such as hypertension, dyslipidemia, diabetes, and obesity, hyperlipidemia.[6, 15, 40]

Up to now, no study has stated any toxic or carcinogenic consequences secondary to policosanol supplementation. In a single take a look at the use of beagle puppies, 180 mg/kg of original policosanol became administered daily for 12 months. The results indicated no histological or biochemical abnormalities in animals receiving the remedy as compared to controls. Moreover, policosanol supplementation did not accelerate tumor boom.[82] Reproductive studies on rats and mice show policosanol at 1,500-times the normal human dose has no negative effect on fertility, reproduction, teratogenesis, or improvement.[83]

Drug Interaction:

Facts from lengthy-time period research in human beings imply that co-administration of nifedipine and other calcium antagonists, angiotensin-converting enzyme inhibitors, β-blockers, diuretics, nitrates, nonsteroidal anti-inflammatory pills, anxiolytics, antidepressants, neuroleptics, oral hypoglycemic pills, digoxin, thyroid hormones, and antiulcer pills is secure;8 Policosanol inhibits platelet aggregation, and can decorate the impact of other anticoagulant medications. While blended with aspirin, policosanol expanded coagulation time in humans.[13] Taking policosanol together with warfarin may boom the chances of bruising and bleeding. Taking policosanol with diabetes medications might reason blood sugar to drop too low. Policosanol might increase the blood stress decreasing results of nitroprusside; this could motive blood strain to move too low. Taking policosanol along with Beta-blockers medication that lower blood pressure.[84]

CONCLUSION:

In this review paper we discussed the general information, isolation methods such as saponification method, solvent extraction, trans-esterification and molecular distillation, supercritical carbon dioxide extraction, ultrasonic assisted extraction, etc. and pharmacological uses of policosanol in various diseases with their safety profile. Policosanol is widely distributed naturally and can be easily isolated and purified from rice bran, sugarcane, apples, grapes etc. Policosanol is safe when it given in alone or combination with other drugs such as statins, or other drugs for treatment of various diseases. Policosanol has been containing the long chain aliphatic, alcoholic mixture of components such as octacosanol, docosanol, tetracosanol, hexacosanol, triacontanol, dotriacontanol, tetraatriacontanol. Policosanol particularly used for the traditional medicine since is a natural product which harvested from food or plants, without serious side effects. Policosanol mainly used in the treatment of hyperlipidemia, neurodegenerative diseases such as Alzheimer's disease, Parkinson's disease, brain stroke, diabetes, obesity, inhibition of platelet aggregation, atherosclerosis cardiovascular diseases etc. There are many therapeutic benefits of policosanol; the main signaling pathways involved in its physiological actions include AMPK, MAPK and PI3K/Akt which have been reported so far. Other than molecular mechanisms of lipid-lowering by inhibiting the HMG-coA reductase enzyme, and anti-atherosclerosis AMPK, MAPK/Erk together with anti-inflammatory effects in the gut via MAPK/NF-κB/AP-1 has been clearly identified, the molecular mechanisms for other physiological effects of policosanol remains unknown. octacosanol can be developed as a good replacement for the synthetic antibiotics named tiamulin. Policosanol affects some physiological performances like energy-metabolism promotion and the laying of eggs hence it also can be a dietary supplement in animal feedstock. Policosanol is shown to be a safe, well- tolerated and effective against various metabolic syndromes. Thus, using this natural product will go a long way in reducing the burden and economic consequences of the syndrome.

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