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A review on dietary phytosterols: Their occurrence, metabolism and health benefits

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ABSTRACT

Phytosterols are steroid compounds present in plants which are similar to cholesterol in structure and functions. Several animal and human studies show that phytosterols lower plasma total and LDL-cholesterol levels. It is generally accepted that cholesterol-lowering effect of phytosterols is due to direct inhibition of cholesterol absorption, through displacement of cholesterol from mixed micelles. Saturated phytosterols (stanols) are found to be more efficient in lowering cholesterol levels than sterols (unsaturated). Phytosterols are structurally very similar to cholesterol except that they always contain some substitutions at the C24 position on the sterol side chain. Plasma phytosterol levels in mammalian tissues are normally very low due to poor absorption from the intestine and faster excretion from the liver compared to cholesterol. Phytosterols can be metabolized in the liver of mammals into C21 bile acids instead of the normal C24 bile acids. Phytosterols may produce health benefits in animals/humans such as reduction of cholesterol levels with decreased risk of coronary heart diseases, anti-inflammatory activities, induction of apoptosis in cancer cells, disease prevention and treatment. However, few adverse effects of phytosterols occur in small group of individuals with phytosterolemia, an inherited lipid disorder and they may cause decrease in plasma levels of nutrients such as carotenoids. In conclusion, phytosterols and their derivatives have several biological activities which promote the health of man and animals, so their consumption should be encouraged in the population.

Keywords: Phytosterols, Safety, Efficacy, Functional foods, Metabolism

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INTRODUCTION

The term “Cholesterol” was derived from the ancient Greek word “Chole” – for bile and “Stereos” – for solid, followed by the chemical suffix “–ol” for an alcohol. It is an organic molecule, which is a sterol (or a modified sterol) and classified under lipid molecules [1]. It is an essential structural component of membranes of animal cells which is required to obtain proper membrane permeability and fluidity. Apart from its importance within cells, cholesterol also serves as a precursor for the biosynthesis of steroid hormones, bile acids and vitamin D [2]. Although cholesterol is the predominant sterol in animals including humans, a variety of sterols are found in plants, known as phytosterols.

Phytosterols, which include plant sterols and stanols, are steroid compounds that occur in plants and are similar to cholesterol but vary only in carbon side chains and/or presence or absence of a double bond, and may lower blood cholesterol levels [3, 4]. Thus, phytosterols are considered as plant cholesterols; for they are plant-derived lipid compounds that are similar in structure and functions to cholesterol [5]. Plant cholesterols are naturally-occurring in the parts of all plants and there are claims by researchers that they may promote the health of man and animals when consumed regularly for a reasonable period either in natural foods or in enriched food supplements.

Therefore, the aim of this study is to conduct a survey of scientific literatures about the occurrence of phytosterols, their bioavailability and metabolism, biological activities and health benefits. In addition, to obtain information about the safety and any notable adverse effect associated with the consumption of these phytochemicals.

Types of Phytosterols

Phytosterols have been classified into two: (1) *Sterols*, which have a double bond in the sterol ring, so are unsaturated compounds (figure 1); and (2) *Stanols*, which lack a double bond in the sterol ring, so are saturated molecules (figure 2). The most abundant sterols in plants and human diets are sitosterols and campesterols. Stanols are also present in plants, but they form only 10% of total dietary phytosterols.

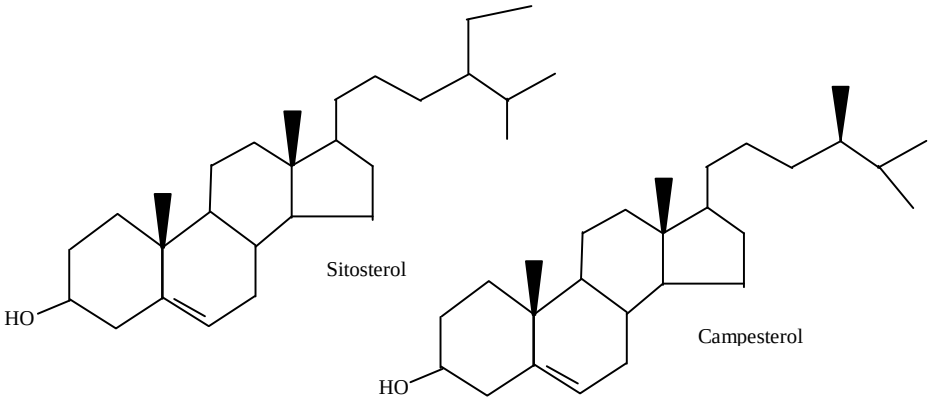


Fig. 1: Chemical structures of sterols

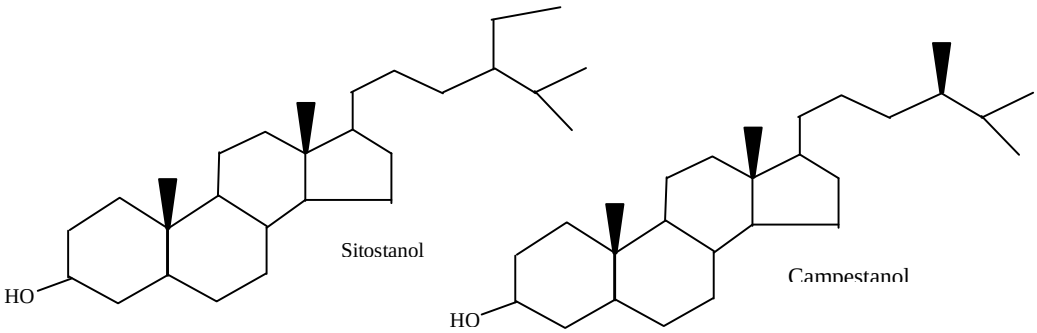


Fig. 2: Chemical structures of Stanols

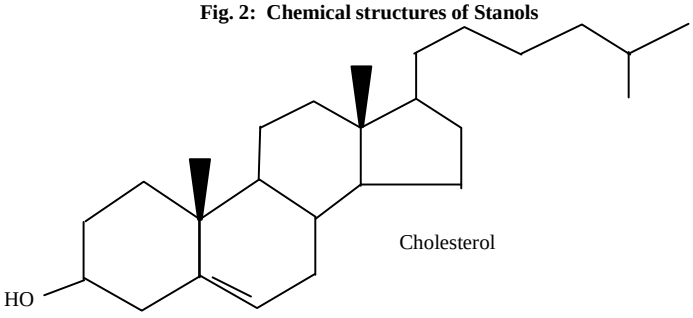


Fig. 3: Chemical structure of Cholesterol

NB: *By removing carbon 24^2 on the steroid skeleton, campesterol is formed. Removing an hydrogen atom from carbons 22 and 23 yields stigmasterol (stigmasta-5,22-dien-3β-ol). By removing carbons 24^1 and 24^2 from the steroid skeleton, cholesterol is obtained. By hydrogenating the double bond between carbons 5 and 6 in β-sitosterol, β-sitostanol is obtained. By hydrogenating the double bond between carbons 5 and 6, and removing carbon 24^1 of the steroid skeleton, campestanol is obtained. Esterification of the hydroxyl group at carbon 3 with fatty/organic acids or carbohydrates results in plant sterol esters. i.e. oleates, ferulates and (acyl) glycosides. Removing carbon 24^2 and hydrogens from carbons 22 and 23, and inverting the stereochemistry at C-24 yields brassicasterol. Further removal of hydrogen atoms from carbons 7 and 8 from brassicasterol yields ergosterol. It is important to note that ergosterol is not a plant sterol. Ergosterol (ergosta-5,7,22-trien-3β-ol) is a component of fungal cell membranes, serving similar functions in fungi as cholesterol in animal cells. It is a cholesterol derivative and the principal sterol of fungi and yeast, so is classified as mycosterol. It is an important molecule in these lower organisms because when irradiated with U.V. light, vitamin D_2 and other derivatives are obtained [51].*

OCCURRENCE OF PHYTOSTEROLS

The richest naturally–occurring sources of phytosterols are vegetable oils & their products. They can be present in the free form and as esters of fatty acid/cinnamic acid or as glycosides. The bound form is usually hydrolyzed in the small intestine by pancreatic enzymes [52]. Nuts, which are rich in phytosterols, are often eaten in smaller amounts, but can significantly contribute to total phytosterol intake. Cereal products, vegetables, fruits and berries, which are not as rich in phytosterols, may also be significant sources of phytosterols due to their higher intakes [53]. Thus, phytosterols are mainly found in vegetables oils but smaller amounts are also present in nuts, legumes, grains, cereals, wood pulp and leaves. It was reported that phytosterols are found in all plant foods but the highest concentrations are found in unrefined plant oils, including vegetables, nuts and olive oils [5]. Humans can not synthesis phytosterols, therefore all phytosterols in human blood and tissues are derived from diet, whereas cholesterol in human blood and tissues is derived from the diet and endogenous cholesterols synthesis [6]. Seeds, whole grains and legumes are also dietary sources of phytosterols [7].

Though sterols and stanols are ubiquitous in the plants world but they are most effective when taken with food, so they are now produced commercially to be added to food. They are available under various trade names such as Benecol® and Flora pro.active®. Plant sterols or stanols that have been esterified by creating an ester bond between a fatty acid and the sterol or stanol are known as plant sterol or stanol esters. Esterification makes plant sterols and stanols more fat-soluble, so they can easily be incorporated into fat-containing foods, including margarines and salad dressing. The most commonly occurring phytosterols in human diet are *β-Sitosterol*, *Campesterol* and *Stigmasterol*, which account for about 65%, 30% and 3% of diet contents respectively [13]. The most common plant stanols in the human diet are *Sitostanol* and *Campestanol*, which combined to make up about 5% of dietary phytosterol [14].

ABSORPTION AND METABOLISM

Though various diets contain similar amounts of phytosterols and cholesterol, serum phytosterol concentrations are usually several hundred times lower than serum cholesterol levels in humans [12]. It was reported that less than 10% of dietary phytosterols are systematically absorbed, in contrast to about 50 – 60% of dietary cholesterol [15]. Like cholesterol, phytosterols are incorporated into mixed micelles before they are taken up by enterocytes. Once inside the enterocytes their systemic absorption is inhibited by the activity of efflux transporters, consisting of a pair of ATP-binding cassette (ABC) proteins known as ABCG5 and ABCG8 [6]. ABCG5 and ABCG8 each forms one half of a transporter that secretes phytosterols and unesterified cholesterol from the enterocyte into the interestinal lumen. Phytosterols are secreted back into the intestine by ABCG5/G8 transporters at a much greater rate than cholesterol, resulting in much lower intestinal absorption of dietary phytosterol than cholesterol. Within the enterocytes, phytosterols are not as readily esterified as cholesterol, so they are incorporated into chylomicrons at much lower concentrations. Those phytosterols that are incorporated into chylomicrons enter blood circulation and are taken up by the liver. Once inside the liver, phytosterols are metabolized into cholesterol and other metabolites, by the action of several enzymes and a key enzyme called cholesterol 7∝-hydroxylase into bile acids, and rapidly secreted into bile by hepatic ABC G5/G8 transporters. This enzyme is a regulatory enzyme in bile acids biosynthesis. Even though cholesterol could also be secreted into bile, the rate of phytosterol secretion into bile is greater than cholesterol secretion [16]. Therefore, the low serum concentrations of phytosterols compared to cholesterol can be explained by decreased intestinal absorption and increased excretion of phytosterols into bile.

Sterol Metabolism in Microbivorous Nematodes

Nematodes are among the most numerous and ecologically diverse multicellular organisms inhabiting the planet earth, though they are largely hidden from public view. Although most species are microbivorous, numerous species are economically or medically important parasites of plants and animals. Much has been learnt about the metabolism of sterol in microbivorous nematode species because many of them can be easily propagated in sterile media. In the first investigation of sterol composition in a free-living species, *Turbatrix aceti* (the vinegar eelworm) contained cholesterol, 7-dehydrocholesterol and lathosterol when cultured in a sterile aqueous medium of yeast extract, soy peptone, acetic acid and liver extract. When this medium was supplemented with radiolabeled cholesterol or sitosterol, the 7-dehydrocholesterol from *T. aceti* was radiolabeled, indicating that the nematode metabolized the dietary sterols by introducing a Δ^7-bond (as well as dealkylating the sitosterol at C-$_{24}$). The Δ^{24}-sterol reductase inhibitor, triparanol succinate, was not inhibitory to *T. aceti* but induced an accumulation of desmosterol, as similar inhibitors induce in insects [54].

Many years later, these experiments were extended to involve a sterile culture medium consisting of solvent-extracted yeast extract, haemoglobin, glucose, unextracted soy peptone and supplemented with a specific dietary sterol in a Tween 80 solution. Solvent extraction minimized the contribution of endogenous sterol contaminants within the medium components. When *Caenorhabditis elegans* (a microbivorous nematode) was propagated in such a medium supplemented with radiolabeled sitosterol, its major 4-desmethylsterols were 7-dehydrocholesterol (56% of total sterol), cholesterol (8%), lathosterol (6%) and unmetabolized dietary sitosterol (18%) [55]. Addition of a known inhibitor of Δ^{24}-sterol reductase in insects, 25-azacoprostane hydrochloride, resulted in over 96% of the total nematode sterol (excluding the dietary sitosterol) consisting of Δ^{24} - or $\Delta^{24(28)}$-sterols such as cholesta-5,7,24-trienol, desmosterol, cholesta-7,24-dienol and fucosterol. These latter sterols were detected in inhibitor-untreated nematodes at most in trace quantities. So these four sterols are likely intermediates in the metabolism of sitosterol in C. elegans. The fact that all nematode sterols had the same specific activity as the dietary sitosterol indicated that the compounds were metabolic products of *C. elegans* and that the azacoprostane inhibited the Δ^{24}-sterol reductase of *C. elegans*. In the study conducted to investigate the metabolism of various dietary sterols and the effects of an azasteroid on sitosterol metabolism in the free-living nematode *C. elegans*, it was discovered that the organism not only removes the substituent at C-24 of dietary sitosterol but also possesses the unusual ability to produce significant quantities of 4∝-methylsterols [55].

These experiments were repeated with *C. elegans* propagated in media supplemented with several C-$_{27}$ sterols. This nematode species was able to modify the sterol nucleus in several ways including C-5 hydrogenation, Δ^7- and $\Delta^{9(11)}$-bond formation and $\Delta^7 \rightarrow \Delta^{8(14)}$-bond isomerization. Also, the absence or near absence of cholesterol in stigmasterol-, cholestanol-, lathosterol-, or 7-dehydrocholesterol-fed *C. elegans* indicated that it could not introduce Δ^5-bonds or hydrogenate Δ^7-bonds [56, 57]. The most interesting nuclear transformation of sterols discovered in *C. elegans* was its production of substantial quantities (5 – 15 % of total sterol) of 4∝-methylcholest-8(14)-enol, radiolabeled with the same specific activity as the original dietary sterol. As 4∝-methylation was seen to be a remarkable phenomenon, experiments were performed to determine if the 4∝-methylsterols were artifacts, for instance, by the addition of antibiotics to the medium or incubation of nematode-free medium. All results consistently showed the existence of a pathway for direct 4∝-methylation in *C. elegans*. This is a major pathway in which nematodes differ not only from higher animals and plants but also insects.

Biosynthesis of Phytosterols

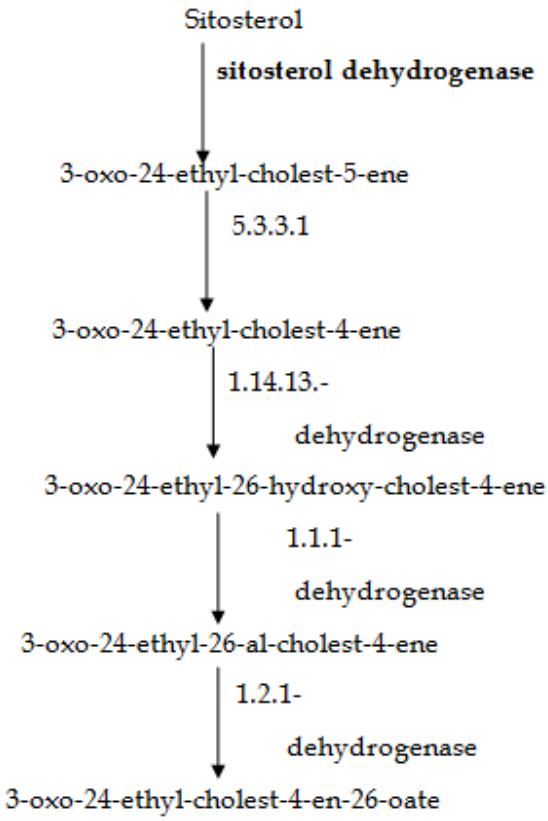
Fungi, algae and protozoa synthesize 24 β-methyl sterols or ergosterols, while plants synthesize 24 β-ethyl sterols such as sitosterols. The sterol methylations are catalyzed by (S)-adenosyl-L-methionine: Δ(24)-sterol methyl transferases (SMT), which are key enzymes in the biosynthesis of plant sterols. Non-photosynthetic organisms do not have these enzymes. Although SMTs from lower organisms and plants appear to be distinct, their mechanistic behavior and mode of sterol transformation seems to be similar [64].

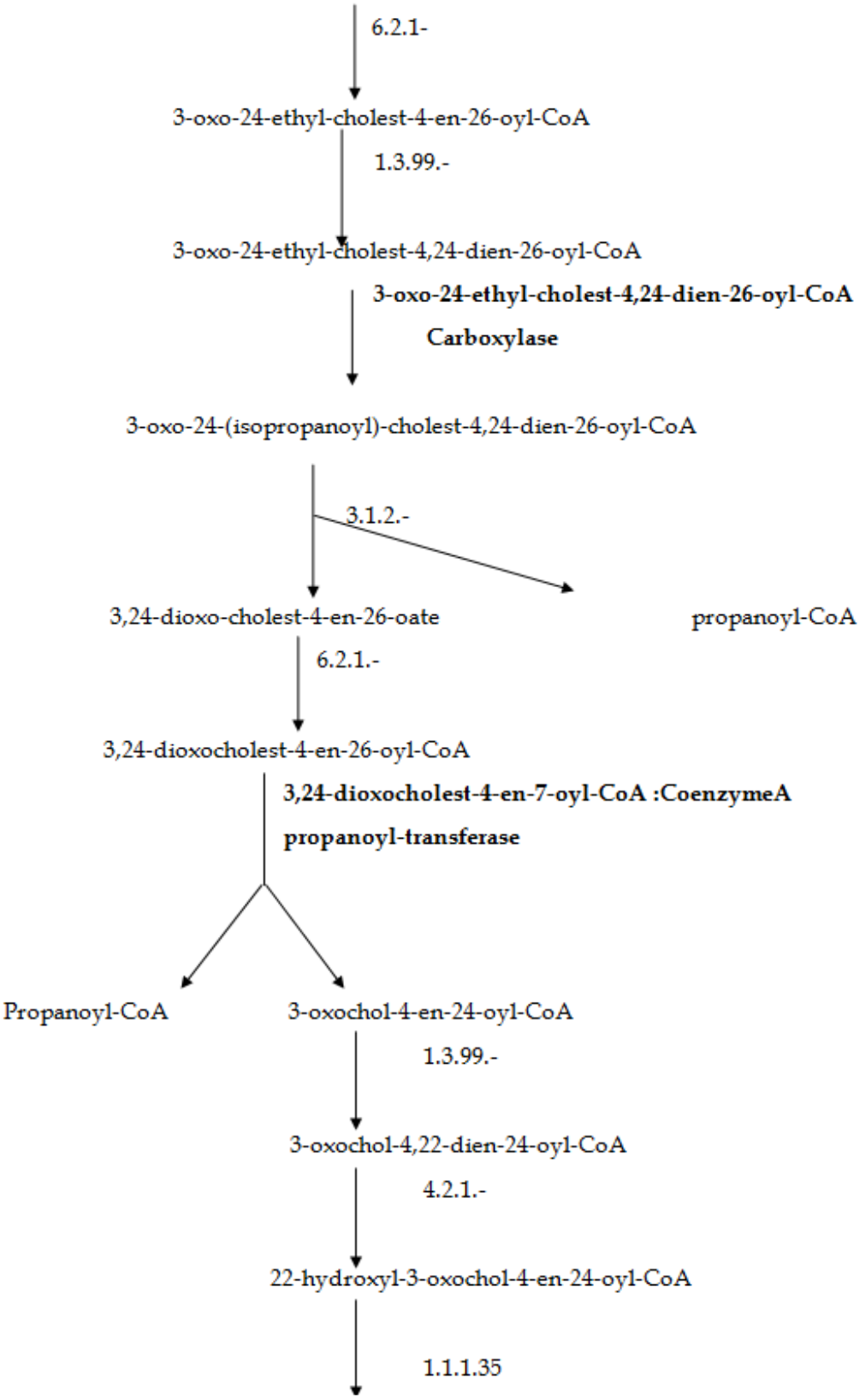
Hydroxymethylglutaryl-CoA reductase (HMG-CoA reductase) regulates the synthesis of mevalonic acid (MVA), a precursor of a myriad of isoprenoid compounds functional in plants cells, with phytosterols representing one class of major importance. Mevinolin, a highly specific competitive inhibitor of HMG-CoA reductase, has been useful as a research tool in studying the regulatory role of HMG-CoA reductase activity for the growth and development of

intact seedlings and cell cultures. The results obtained indicate a primary effect of mevinolin on phytosterol accumulation, whereas other end products of the multi-branched isoprenoid pathway are not affected. Since the mevinolin-induced drop in free sterol accumulation is directly proportional to significant plant growth retardation, it is suggested that HMG-CoA reductase has a rate-limiting role in phytosterol synthesis and normal development of plants [62]. In the yeast, β-sitosterol is converted to stigmasterol by the action of sterol-22-desaturase and $\Delta^{5,7}$-campesterol is also converted to ergosterol by the action of sterol-22-desaturase. Some scientists have constructed a *Caenorhabditis elegans* strain expressing human dehydrocholesterol reductase activity, which enabled the worms to convert exogenous 7-dehydrocholesterol into cholesterol. This transgenic strain was slightly longer-lived and stress-resistant, but showed reduced fecundity [63].

Sitosterol degradation to androstenedione

Early studies showed that many species of micro-organisms of the genera Bacillus, Microbacterium, Mycobacterium, Streptomyces etc were able to degrade sitosterol. The bacterial degradation of animal-derived cholesterol has been studied comprehensively while the degradation of phytosterol is not nearly as well documented. Several intermediates in the side chain degradation pathway were reported over the years from different strains. So it is now concluded that the mode of microbial degradation of the sitosterol side chain proceeds via hydroxylation at C26, followed by oxidation to 3-oxo-24-ethyl-cholest-4,24-dien-26-oyl-CoA. In the next step, bicarbonate is incorporated onto the C28 position, followed by carbon-carbon bond fission, liberating propanoyl-CoA and forming 3-oxochol-4-en-24-oyl-CoA, an intermediate that is also formed during cholesterol degradation [65]. The rest of the pathway is predicted to proceed analogous to cholesterol degradation. Side chain degradation is completed by liberation of a second molecule of propanoyl-CoA, followed by one molecule of acetyl-CoA, resulting in the common sterol degradation intermediate, androst-4-ene-3,17-dione, simply called androstenedione [66, 67].

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Carboxylase
3-oxo-24-(isopropanoyl)-cholest-4,24-dien-26-oyl-CoA
3.1.2.-
3,24-dioxo-cholest-4-en-26-oate
propanoyl-CoA
6.2.1.-
3,24-dioxocholest-4-en-26-oyl-CoA
3,24-dioxocholest-4-en-7-oyl-CoA :CoenzymeA
propanoyl-transferase
Propanoyl-CoA
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1.3.99.-
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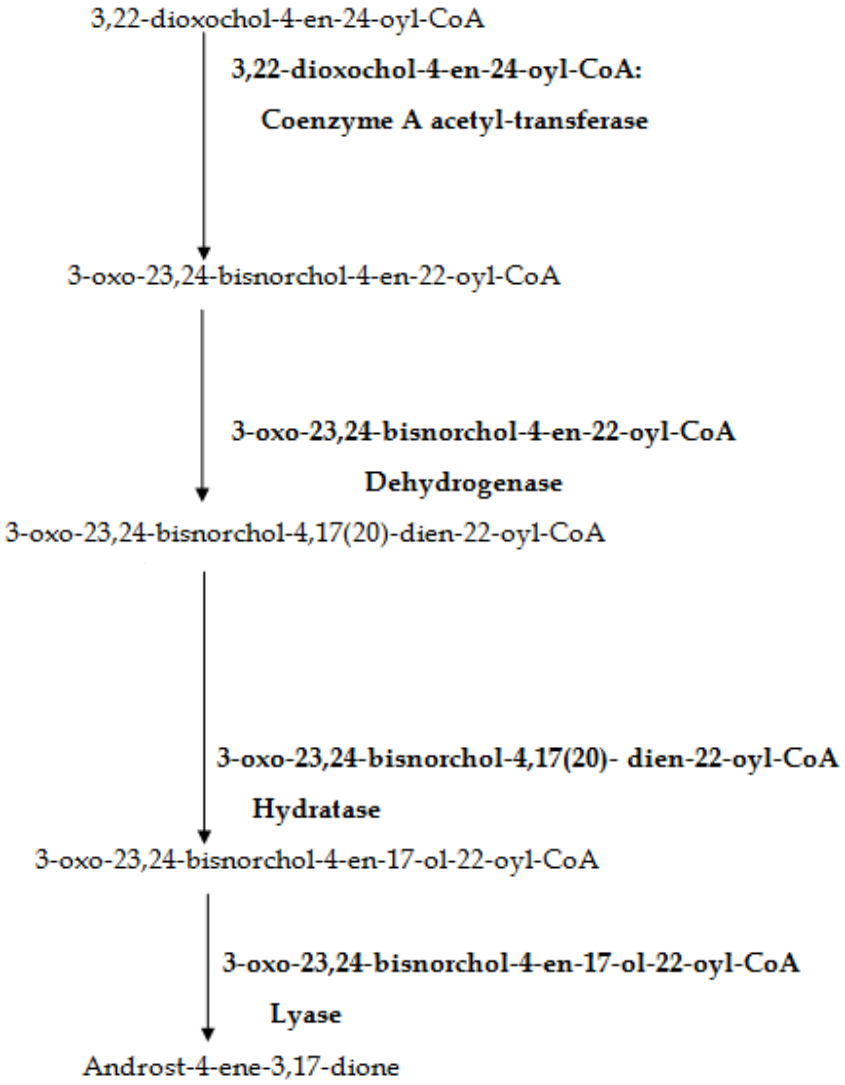

Figure 4: Pathway for Sitosterol degradation to androstenedione.

NB: If the name of an enzyme is shown in bold, there is experimental evidence for this enzyme activity in micro-organisms.

Androstenedione is a common intermediate in both sitosterol and cholesterol degradation, with several important uses. It is also a steroid intermediate used in the pharmaceutical industry for the production of several important anabolic drugs [68].

BIOLOGICAL ACTIVITIES OF PHYTOSTEROLS

Effects on cholesterol absorption and lipoprotein metabolism

The ability of phytosterols to reduce cholesterol levels was first demonstrated in humans in 1953 [17, 18]. It was subsequently marketed as a pharmaceutical product under the name *cytellin*, used for treatment of elevated cholesterol from 1954 – 1982 [19]. Today, it is well established that high intakes of plant sterols or stanols can lower serum total and LDL-cholesterol concentrations in humans [20, 21]. In the intestinal lumen, phytosterols displace cholesterol from mixed micelles and inhibit cholesterol absorption [22]. In humans, the consumption of 1.5 – 1.8 g/day of plant sterols or stanols reduced cholesterol absorption by 30 – 40 % [23]. Tissue LDL–receptor expression was increased in response to decreased cholesterol absorption, resulting in increased clearance of circulating LDL [24]. Decreased cholesterol absorption is also associated with increased cholesterol synthesis, and increasing

phytosterol intake has been found to increase endogenous cholesterol synthesis in humans [25]. In one particular study, the activity of beta-Hydroxy-β-methylglutaryl-CoA reductase (a rate-limiting enzyme of cholesterol synthesis) was increased 2-fold in animals earlier fed β-sitosterol [60]. Despite the increase in cholesterol synthesis induced by increasing phytosterol intake, the net result is a reduction in serum LDL cholesterol concentration. Health Canada reviewed the evidence of 84 randomized controlled trials published between 1994-2007 involving phytosterol supplementation. An average of 8.8% reduction in LDL-cholesterol was observed at a mean intake of 2 grams of phytosterols per day [61]. Therefore, Health Canada concluded that sufficient scientific evidence exists to support a relationship between phytosterol consumption and blood cholesterol lowering. Structure-specific effects of individual phytosterol constituents have recently been shown, where saturated phytosterols were found to be more effective than the unsaturated forms in lowering cholesterol levels [36].

Alterations in cell membrane properties

Cholesterol is an important structural component of mammalian cell membranes, so displacement of cholesterol with phytosterols has been found to alter the physical properties of cell membranes *in vitro* [26], which could potentially affect signal transduction or membrane-bound enzyme activity [27]. Limited evidence from animal model of hemorrhagic stroke suggested that very high intakes of plant sterols or stanols displaced cholesterol in red blood cell membranes, resulting in increased deformability and potentially increased fragility [28]. However, daily phytosterols supplementation (1g/1000kcal) for four weeks did not alter red blood cell fragility in humans [29].

Alteration in testosterone Metabolism

Evidence from animal studies suggests that very high phytosterol intakes can alter testosterone metabolism by inhibiting 5-alpha-reductase, a membrane-bound enzyme that converts testosterone to dihydro-testosterone, a more potent metabolite [30]. Thus, phytosterols might reduce the activity of enzymes involve in testosterone metabolism in male animals. However, it is not known whether phytosterol consumption alters testosterone metabolism in humans. A recent study has shown that no significant changes in free or total serum testosterone concentrations were observed in men who consumed 1.6 g/day of plant sterol esters for one year [31].

Anti-inflammatory Effects

Limited data from cell culture and animal studies suggest that phytosterols may attenuate the inflammatory activity of immune cells, including macrophages and neutrophils [32]. Thus, they may have anti-inflammatory activities in living systems.

Induction of Apoptosis in cancer cells

Unlike normal cells, cancerous cells lose their ability to respond to death signals that initiate apoptosis (programmed cell death). Sitosterols have been found to induce apoptosis when added to cultured human prostate [33], breast [34] and colon cancer cells [35]. Therefore, they may play significant roles in the management and prevention of human cancers.

Disease prevention

Most animal and human studies show that phytosterols reduce serum/or plasma total cholesterol and low density lipoprotein (LDL) cholesterol levels [36]. It was reported that blood cholesterol can be reduced on average by 7 to 10.5% if a person consumes 1.5 to 2.4 grams of plant sterols and stanols every day [37]. Based on available efficacy data, the European Foods Safety Authority (EFSA) concludes that plant sterol and stanol esters have been shown to reduce blood cholesterol and the lowering of blood cholesterol may reduce the risk of coronary heart disease [37]. The food and Drug Administration (FDA) and Health Canada have also adopted similar positions. Numerous clinical trials have found that daily consumption of foods enriched with free or esterified forms of plant sterols or stanols reduce concentrations of serum total and LDL cholesterol [20, 38]. A meta-analysis that combined the results of 23 controlled clinical trials found that the consumption of plant foods providing an average of 3.4 g/day of plant sterols or stanols decreased LDL-cholesterol concentrations by about 11% [39]. The results of numerous intervention trials suggest that a 10% reduction in LDL cholesterol induced by medication or diet modification could decrease the risk of CHD by as much as 20% [40].

A cross-sectional study in the UK found that dietary phytosterol intakes were inversely related to serum total and LDL cholesterol concentrations, even after adjusting for saturated fat and fiber intake [14]. Even though more research is needed, available research findings suggest that dietary intake of phytosterols from plant foods could have an important impact on cardiovascular health. Thus, the US Food and Drug Administration (FDA) has

authorized the use of health claims on food labels indicating that regular consumption of foods enriched with plant sterols or stanol esters may reduce the risk of heart disease [41]. Limited data from animal studies suggest that very high intakes of phytosterols, particularly sitosterol, may inhibit the growth of breast and prostate cancers [42, 43]. Some epidemiological studies have found that higher intakes of plant foods containing phytosterols are associated with reduced cancer risk, however it is not certain whether the protective factors are phytosterols or other compounds in the plant foods. Nevertheless, it is reported that phytosterols may inhibit lung, stomach, ovarian and breast cancers [58]. Scientific research has shown that 24-Epibrassinolide, a brassinosteroid, modulates superoxide dismutase, catalase and glutathione peroxidase activity [59]. Generally, those that would benefit most from phytosterols intake are those who have high plasma cholesterol levels and are at risk of developing cancers or coronary heart diseases.

Disease Treatment

Benign Prostatic Hyperplasia (BPH) is the term used to describe a non-cancerous enlargement of the prostate. The enlarged prostate may exert pressure on the urethra, resulting in difficulty urinating. In a six-month study of 200 men with symptomatic BPH, 60 mg/d of a beta-sitosterol preparation improved symptoms, increased peak urinary flow, and decreased post-void residual urine volume compared to placebo [44]. However, relatively few controlled studies have examined the efficacy of phytosterol supplements in men with symptomatic BPH.

Safety

In the United States, plant sterols and stanols added to a variety of food products are generally recognized as safe (GRAS) by the FDA. The scientific committee on foods of the EU also concluded that plant sterols and stanols added to various food products are safe for human use [45]. However, the committee also recommended that intakes of plant sterols and stanols from food products should not exceed 3 g/day because there is no evidence of health benefits at higher intakes and there might be undesirable effects when they are consumed in high amounts.

Adverse Effects

Phytosterols are usually well-tolerated, however nausea, indigestion, diarrhea and constipation have occasionally been reported [44]. So far few adverse effects have been associated with regular consumption of plant sterols or stanols for up to one year.

Sitosterolemia (Phytosterolemia)

Sitosterolemia, also known as “Phytosterolemia”, is a very rare hereditary disease that results from inheriting a mutation in both copies of the ABC G5 or ABC G8 genes [46]. Individuals who are homozygous for a mutation in either transporter protein have elevated serum phytosterol concentrations due to its increased intestinal absorption and decreased biliary excretion. Though, serum cholesterol concentrations may be normal or only mildly elevated, individuals with sitosterolemia are at higher risk for premature atherosclerosis. Therefore, people with sitosterolemia should avoid foods or supplements with added plant sterols [20].

Pregnancy and Lactation

Plants sterols or stanols added to foods or supplements are not recommended for pregnant or breastfeeding women because their safety has not been studied [20]. At present there is little or no evidence that high dietary intakes of naturally-occurring phytosterols, such as consumed by vegetarian women, could adversely affect pregnancy or lactation.

Phytosterol-Drug Interactions

The LDL cholesterol-lowering effects of plant sterols or stanols may be additive to those of HMG-CoA reductase inhibitors (Statins) [46]. The results of controlled clinical trials suggest that consumption of 2 – 3 g/day of plant sterols or stanols by individuals on statin therapy may result in an additional 7 – 11% reduction in LDL cholesterol, an effect comparable to doubling the statin dose [47]. Another study showed that consumption of 4.5 g/day of stanol esters for eight weeks did not affect prothrombin time (INR) in patients on warfarin [48].

Phytosterol-Nutrient Interactions

Fat-soluble vitamins (Vitamins A, D, E & K) - the effect of plant sterols and stanols on fat-soluble vitamins status have also been studied in clinical trials because they are known to decrease cholesterol absorption and serum LDL cholesterol concentrations. Plasma vitamin A (retinol) concentrations were not affected by plant stanol or sterol esters consumption for up to one year [21, 31]. The majority of studies found no changes in plasma vitamin D (25-

hydroxyvitaminD_3) concentrations, however one placebo-controlled study in individuals consuming 1.6 g/day of sterol esters for one year observed a small (7%) but statistically significant decrease in plasma 25–hydroxyvitamin D_3 concentration [31]. There is little evidence that plant sterol or stanol consumption adversely affects vitamin K status. Consumption of 1.6 g/day of sterol esters for six months was associated with a non-significant (14 %) decrease in plasma vitamin K_1 concentrations but carboxylated osteocalcin, a functional indicator of vitamin K status, was unaffected [31].

Carotenoids - Dietary carotenoids are fat–soluble phytochemicals that circulate in lipoproteins. A number of studies have observed 10 – 20% reductions in plasma carotenoids after short–term and long–term consumption of plant sterol- or stanol- enriched foods [21]. It is not clear whether reductions in plasma carotenoids concentrations could cause any health risks but several studies have found that increasing intakes of carotenoid-rich fruits and vegetables can prevent phytosterol-induced decrease in plasma carotenoids [49]. In one case study, advice to consume five daily servings of fruits and vegetables, including one serving of carotenoid–rich vegetables, was enough to maintain plasma carotenoid levels in people consuming 2.5 g/day of plant sterol or stanol esters [50].

CONCLUSION

There are scientific evidences to support the fact that phytosterols and their derivatives have several biological activities which promote the health of animals, humans and micro-organisms with only few adverse effects, such as occur in phytosterolemia, a rare genetic disorder. These health benefits include reduction of plasma total and LDL-cholesterol levels, which decrease the risk of cardiovascular diseases; anti-inflammatory activities; prevention of colon, breast and prostate cancers, and treatment of benign prostatic hyperplasia. Therefore, regular consumption of plant sterols and stanols in natural foods not exceeding 3 g/day is considered healthy to man and animals.

It is therefore recommended that future work should focus on; better delivery of phytosterols present in natural foods into cells of living organisms, and randomized controlled clinical trials in humans, to determine if cholesterol-lowering activity of phytosterols could reduce risk of cardiovascular diseases, and if the decrease in absorption of fat-soluble nutrients such as carotenoids by phytosterols could cause any health risk.

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