Gamma Oryzanol—Plant Sterol Supplementation: 
Metabolic, Endocrine, and Physiologic Effects

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The use of gamma-oryzanol and phytosterols is gaining popularity among various athletic populations. These compounds are being consumed in the belief that they elicit anabolic effects ranging from increased testosterone production and release to stimulating human growth hormone release. However, published scientific studies suggest that these compounds are poorly absorbed. Furthermore, animal studies indicate that when these compounds are injected subcutaneously or intravenously, they induce antianabolic or catabolic activity. Normally, less than 5% of orally consumed phytosterols are absorbed from the intestinal tract, with the majority being excreted in the feces. Intravenous or subcutaneous injections of gamma-oryzanol in rats have been shown to suppress luteinizing hormone release, reduce growth hormone synthesis and release, and increase release of the catecholamines, dopamine and norepinephrine, in the brain. Although it hasn't been directly measured, this metabolic milieu, if accurate, may actually reduce testosterone production.

Oryzanol was first isolated from rice (Oryza stavia) bran oil by Kaneko and Tsuchiya (15) in the early 1950s. During their studies, a number of lipid fractions were isolated from rice bran oil; the third (gamma) fraction isolated was oryzanol (15). Its chemical composition was later identified as a mixture of ferulic acid esters of various plant sterols (4). The specific group of phytosterols that comprise oryzanol are ferulates of campesterol, stigmasterol, β-sitosterol, cycloartenol, and cycloartenol. The oryzanol fraction of rice bran oil amounts to 1.3–2.6% of the total oil or 20–30% of the unsaponifiable material (21). These same nonferulic-acid-esterified phytosterols are also found in the lipid fraction of many other plants, and subsequently can be identified in various vegetable oils and products.

The phytosterol base of these ferulic acid esters are structurally similar to cholesterol, with differences occurring primarily in the side chain. Campesterol has an extra methyl group at the C-24 position while β-sitosterol and stigmasterol have an extra ethyl group at the C-24 position. Cycloartenol is the most structurally different from cholesterol, with a number of extra methyl groups and the
Figure 1 — Chemical structure of (a) cycloartenol, (b) cholesterol, and (c) ferulic acid.

formation of a ring structure between C-9 and C-10. The chemical structure of cycloartenol, cholesterol, and ferulic acid is shown in Figure 1. The structural similarities between oryzanol, phytosterols, and cholesterol have led to numerous theories and claims regarding the physiologic, metabolic, and performance effects of these compounds following ingestion.

**Physiologic, Metabolic, and Performance Claims**

The physiologic, metabolic, and performance claims for gamma-oryzanol are quite broad but focus mainly on the hormone system. Below is a short list of the more common statements and claims made in various product guides (i.e.,
Power-Built brochure, Bricker Labs; Product Profile, Ultimate Nutrition Products, Inc.; Sports Nutrition, National Health Products) regarding the effects of exogenous oryzanol supplementation:

- That gamma-oryzanol is an extract from a rare variety of the oryza plant, which has an effect on the intermediary metabolism as well as organ interrelationships, and that it also raises the natural testosterone levels;
- That gamma-oryzanol stimulates the hypothalamus, causing release of the Growth Hormone Releasing Hormone, which influences the release of Human Growth Hormone (HGH). Gamma-oryzanol is a natural steroid alternative that develops increased lean muscle mass and definition;
- That β-sitosterol, an oryzanol component, has a chemical structure that can be readily converted into androgens, resulting in anabolic enhancement.

Neither oryzanol nor phytosterols are currently recognized as food additives by the U.S. Food & Drug Administration (FDA). Rice bran oil is recognized as an "indirect food additive" by the FDA for adhesives, paper materials, and glue used in food packaging (5).

Dietary Intake and Absorption

Sterols of some type are present in virtually all foods containing a lipid fraction. Cholesterol is the most common sterol in foods of animal origin. However, as previously mentioned, sterols are also found in the lipid fraction of plants and thus are consumed with vegetables and vegetable oils. Connor (2) has estimated that the typical American diet supplies approximately 180 mg of plant sterols each day. The main sterols found in the diet include sitosterol, stigmasterol, and campesterol, with sitosterol being the single greatest component (2).

Since it is found in the lipid fraction of rice, oryzanol is consumed in much lower quantities. For example, one cup of white rice contains 200 mg of fat, of which approximately 4 mg would be oryzanol. Since brown rice contains more fat, one cup would contain approximately 18 mg of oryzanol.

In general, plant sterols and oryzanol are poorly absorbed from the intestinal tract. A number of early studies (13, 14, 17) suggested that the extent of absorption of phytosterols (mainly sitosterols) ranged from 22 to 35% of the total amount ingested by rats. However, these studies calculated absorption as the simple difference in the total quantity of sterol ingested minus the amount of sterol recovered in the feces. Gould et al. (8) found that less than 5% of tritium labeled β-sitosterol was absorbed when a 50-mg dose was ingested by healthy humans. Less than 2% of sitosterol or fucosterol were absorbed following the intragastric administration of 25 mg of each in rats (12).

Other studies have observed that this apparent difference in absorption is due to significant degradation of the sterol structure in the gastrointestinal tract (10). The degree of phytosterol destruction in the gastrointestinal tract can apparently be affected by the type of diet consumed. Consumption of a liquid diet containing 3,000 mg of a plant sterol mixture (65% β-sitosterol, 30% campesterol, and 5% stigmasterol) during a sterol balance study resulted in a 39 to 59% recovery rate of intact sterol from the feces (3). When ethyl cellulose was added to the liquid diet or when a mixed solid food diet was consumed, recovery of the
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The absorption of plant sterols from the feces was improved to 100% (3). Denbesten et al. suggest that the increased destruction of the sterols results from intestinal bacteria seeking an alternate source of carbon when their normal source is not supplied with the fiber or solid food fraction.

The degree of plant sterol absorption also is not significantly influenced by the concentration in the diet. When rats consumed tritium labeled sitosterol at 0.1, 0.5, and 5.0% of the diet for 2 weeks, similar amounts of total sterol absorption were found (7). Salen et al. (19) found a significant decrease in the percent of β-sitosterol absorbed with increasing dietary concentrations. When dietary sterol intake was increased from 242 mg to 1,909 mg in different subjects, the percent absorbed was reduced from 5.2 to 0.6%. Salen et al. also demonstrated that a sixfold to sixtyfold increase in sitosterol intake resulted in less than a twofold increase in plasma sterol concentration (19).

The poor absorption characteristics of phytosterols and oryzanol are one reason they are effective inhibitors of cholesterol absorption. Some early research has suggested that since plant sterols are structural analogs of cholesterol, they compete with cholesterol during some aspect of the absorption process (23). However, Ikeda et al. (12) have found that plant sterol inhibition of cholesterol absorption may not be associated with competitive binding of brush border membranes. In vitro studies suggest that sitosterol reduces the solubility of cholesterol in taurocholate micelles, thus causing displacement of the cholesterol from the bile salt micelles (12).

Metabolic and Endocrine Effects

Few published human or animal studies have examined the metabolic fate and effect of plant sterols and oryzanol following absorption. Gould et al. (8) studied the blood and tissue distribution of tritium labeled β-sitosterol in normal subjects and terminal patients. Their data indicated that sitosterol, once absorbed, is distributed in blood, plasma, red cells, and various tissues (i.e., liver, lungs, coronary artery, stomach, spleen, adipose tissue) in a pattern similar to cholesterol. Other research has demonstrated that phytosterols are converted into the same major bile acids as cholesterol; however, they (primarily sitosterol) appear to be more rapidly secreted into the bile (19). It has been hypothesized that the reason for the sterols’ rapid secretion into bile is due to the fact that they are slowly esterified, if at all (19). Thus phytosterols are poorly absorbed and rapidly excreted by the body.

Although no research is available on the absorption characteristics of oryzanol per se, there is no reason to believe it would be absorbed differently from the phytosterols. It is possible the absorption rate would be slower for oryzanol, considering the larger size of this esterified molecule.

No scientific evidence has been published suggesting that phytosterols or oryzanol possess anabolic-androgenic activity. The few animal studies that have examined endocrine effects of injected oryzanol suggest it may actually suppress anabolic activity. When healthy male rats were given a single intravenous injection of 5 mg gamma-oryzanol in conjunction with luteinizing hormone releasing hormone (LHRH), serum luteinizing hormone (LH) levels were significantly suppressed over twofold when compared to placebo-LHRH controls (26). LH in the male of a species is important because it increases the synthesis of testosterone.
by acting on the Leydig cells located between the seminiferous tubules (16). In the same study, the intravenous injection of 5 mg gamma-oryzanol had no effect on serum growth hormone (GH) or thyroid-stimulating hormone (TSH) and was a weak inhibitor of prolactin in female rats (26).

Ieiri et al. (11) examined the effect of oryzanol injection on growth hormone synthesis and release. One hour following the subcutaneous injection of 20 mg/kg gamma-oryzanol, GH synthesis was significantly suppressed and a trend for GH release to be reduced, compared with an oil control, was observed. This same study demonstrated that a subcutaneous injection of gamma-oryzanol increased release of the catecholamines dopamine (DA) and norepinephrine (NE) in the medial basal hypothalamic region of the rat brain. Since these catecholamines are primarily catabolic in nature, this parallels the effect of oryzanol on LH.

The mechanism by which injected gamma-oryzanol creates a potentially catabolic or antianabolic state has not been investigated. However, the results of these studies (7, 11, 19, 23, 24, 26) suggest an interesting possibility (Figure 2).

Figure 2 — Flow diagram of hormonal regulation of testosterone production. (−) represents inhibitory control points that reduce testosterone production. LH is required in the initial rate limiting step of cholesterol conversion to testosterone.
The hypothalamus produces and releases LHRH, which stimulates the pituitary to secrete LH. LH regulates the synthesis of testosterone from cholesterol in the testis by controlling the initial rate-limiting step, that is, the conversion of cholesterol to pregnenolone (16). In the normal man, testosterone negatively feeds back on the pituitary to make the gland less sensitive to LHRH stimulation. This control mechanism helps maintain a normal circulating testosterone level in men.

It is possible that the gamma-oryzanol, due to its sterol structure, has the same negative feedback effect on the pituitary as testosterone. This would explain the decrease in LH release previously mentioned when 5 mg of gamma-oryzanol were injected intravenously in male rats (26). Administration of as little as 6 mg exogenous androgen has been shown to completely suppress LH secretion by the pituitary (9). The increased release of DA and NE may also influence the release of LH. These catecholamines are believed to be mediators involved in the release of LHRH by the hypothalamus (16). Thus, abnormally high levels of DA and NE in the brain may suppress LHRH release. It is unclear why the gamma-oryzanol had a suppressive effect on GH synthesis and release, especially since DA is thought to be associated with the release of GH (16).

Whether effects of gamma-oryzanol on the rat are due to the sterol portion of the compound or the ferulic acid was not determined. However, it appears that the sterol portion would have the greatest potential effect. Administration of 100 mg of ferulic acid to Holstein heifers did not influence serum concentrations of LH or thyroid hormones, and only slightly but not significantly elevated GH (6). When given to rats, ferulic acid produced antiandrogenic activity on the prostate but not the testis (18).

**Medical Risks of Consuming Phytosterols and Oryzanol**

The toxicity of these compounds has not been extensively evaluated, but is apparently minimal because of their extremely poor absorption. However, some reports indicate that some medical risks may be associated with the consumption of these compounds. Case reports have documented xanthomatosis occurring in patients with lipid-storage disease due to excessive absorption of the phytosterols β-sitosterol and campesterol (1, 22). In one report (1), the intestinal absorption of β-sitosterol in these patients was found to be approximately 25%, which is significantly higher than the normal rate (<5%) noted in healthy humans and reported in other studies (8, 17). It is possible that the poor absorption characteristics of these compounds is a natural defense mechanism, because large doses have been chronically consumed without complication (20). Chronic schizophrenic patients who were given 300 mg of gamma-oryzanol daily for 16 weeks for treatment of dyslipidemia had no negative side effects (20).

In vitro studies with IgM-hemolysin-sensitized sheep erythrocytes suggest that the phytosterols stigmasterol, campesterol, and β-sitosterol may disrupt the immune system (25). In these studies, stigmasterol was found to elicit the most potent anticomplement activity of the three phytosterols investigated.

**Conclusions**

Plant sterols (phytosterols) and oryzanol (ferulic acid esters of plant sterols) are found in the lipid fraction of a variety of plants and vegetables. A typical American diet supplies approximately 180 mg of phytosterols each day. Daily intake
of oryzanol is dependent mainly on the amount and type of rice consumed and is most likely in the range of 4 to 18 mg.

Phytosterols and oryzanol are poorly absorbed from the intestinal tract. Normally less than 5% is absorbed; the majority are excreted in the feces. It also has been determined that dietary concentration has little influence on absorbability. A sixtyfold increase in dietary sitosterol intake resulted in less than a twofold increase in plasma sterol concentration.

In general the metabolic, physiologic, and performance statements and claims made regarding phytosterols and oryzanol are not supported by scientific studies. Oryzanol and phytosterols have not been shown to elicit anabolic-androgenic activity. In fact, much of the animal work involving oryzanol suggests that it actually may create a catabolic or antianabolic state. Intravenous or subcutaneous injections of gamma-oryzanol in rats have been shown to suppress LH release, reduce GH synthesis and release, and increase the release of the catecholamines DA and NE. Ferulic acid also has been shown to produce antiandrogenic activity on the prostate in rats. However, since absorption of these compounds is poor, it is doubtful that oral consumption would induce these metabolic changes.

The medical risks of consuming phytosterol and oryzanol are apparently minimal because of their poor absorption characteristics. However, severe xanthomatosis has been documented in patients with lipid-storage disease due to abnormally high absorption rates of the phytosterols β-sitosterol and campesterol. In addition, in vitro studies have suggested that certain phytosterols may suppress immune system response.

References


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