Unsaponifiables in rice bran oil under study

Robert Nicolosi, University of Lowell, reported on the progress of studies with rice bran oil to the USA Rice Council in Houston, Texas, on March 23, 1990, suggesting that unsaponifiable components of the oil may be the key factor in healthful effects attributed to the oil. This article, based on that presentation, was prepared at the request of INFORM Associate Editor Frank Orthoefer.

Numerous studies have shown that diets enriched in saturated fats compared to polyunsaturated fats raise serum total cholesterol and, in particular, low density lipoprotein (LDL) cholesterol (1–3). Similarly, it has been known for nearly three decades that polyunsaturated vegetable oils have a hypcholesterolemic effect in humans (4–6). The explanation for these effects of types of dietary fat on serum cholesterol levels has been attributed to the concentration of dietary saturated and polyunsaturated fatty acids and, to a lesser extent, to dietary cholesterol (1,7). The predictive equations of Keys et al. (8,9) and Hegsted et al. (10) demonstrated that, gram for gram, saturated fatty acids raise serum cholesterol levels twice as effectively as polyunsaturated fatty acids lower them. These same predictive equations also show that monounsaturated fatty acids raise serum cholesterol levels twice as effectively as polyunsaturated fatty acids lower them. These same predictive equations also show that monounsaturated fatty acids are neutral and have no specific effect independent of replacing saturated fatty acids. More recent studies in humans by Mattson and Grundy (11), Mensink et al. (12), McDonald et al. (13), Sirtori et al. (14) and Dreon et al. (15) have demonstrated that replacement of dietary saturated fatty acids by monounsaturated fatty acids resulted in reductions of LDL cholesterol which were equal to (11,13,15), less than (14), or greater than (12) those associated with polyunsaturated fat intake.

The mechanisms involved in the hypolipidemic effects of these unsaturated fatty acids are not well understood although more recent studies suggest that polyunsaturated fatty acids may prevent the down regulation of LDL receptor activity by saturated fatty acids and cholesterol (16–19). How the various dietary fatty acids mediate their effect on LDL receptor activity is not well established although very recent studies suggest that alterations in membrane
fluidity brought on by the different degrees of diet-induced fatty acid saturation of membrane lipid may be important (20-24).

The diet effects on high density lipoprotein (HDL) cholesterol levels remain equally inconsistent as studies either showed reductions (11, 14) or no change (12, 13, 15) in HDL when saturated fatty acids were replaced by polyunsaturated compared to monounsaturated fatty acids.

Although the fatty acid components in the diet are thought to be the primary determinant of diet-induced hypercholesterolemia, a role for certain components of the unsaponifiable fraction of dietary oils in influencing serum cholesterol levels also has been advocated. For example, in a review article by Grundy (25), observations were cited from the recent investigations by Grundy and Mok (26), Lees et al. (27) and Heimann et al. (28) which indicated that unsaponifiable sterols such as phytosterols can have significant effects on LDL cholesterol levels even at relatively low intakes. Recent studies by Qureshi et al. (29-31) also suggest that tocotrienols, an unsaponifiable component of palm oil, inhibit cholesterol synthesis and lower serum cholesterol levels in various animal models. In one study, the feeding of an unsaponifiable fraction of soybean oil was hypocholesterolemic in primary type II hyperlipoproteinemia (32). Similarly when the unsaponifiable fraction of soybean sterols was further purified and fractionated, both cycloartenol and 24-methylene cycloartenol, which are the main constituents in soybean oil unsaponifiable matter, reduced plasma cholesterol and enhanced cholesterol excretion when fed to rats (33).

Particularly germane to this discussion is the finding that rice bran oil contains an unusually high content of unsaponifiable matter (up to 4.4%) which is several times greater than most other vegetable oils. In addition, rice bran oil, depending on source and degree of processing, can contain up to 20% saturated fatty acids and approximately equal amounts of polyunsaturated (40%) and monounsaturated fatty acids (40%), a fatty acid profile quite different from other often-utilized hypocholesterolemic vegetable oils (Table 1). Equally important is the recently reported studies in which the hypocholesterolemic action of rice bran oil has been attributed to its unsaponifiable fraction. For example, Sharma and Rukmini (34) showed that rice bran oil fed to rats at a 10% level significantly lowered total cholesterol upon addition of the triterpene alcohol oryzanol to the diet. These changes in lipoprotein cholesterol levels were associated with rather striking decreases in liver cholesterol content (30%) in rats fed rice bran oil compared to groundnut oil. Thus, these two rat studies suggest that changes in lipoprotein cholesterol levels in response to the feeding of some

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<td>Distribution of the Major Fatty Acids of Butter and Various Dietary Oils (%)</td>
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acid nature of coconut oil and the sparse information on peanut oil (36) used as the comparative oil.

More recently, our laboratory has investigated the effects of rice bran oil in nonhuman primates fed anywhere from 0% to 35% of calories as fat as part of a blend of several vegetable oils (37) (manuscript in preparation). Animals were rotated through nine different diet treatments of 8-weeks duration each and measurement of serum total, VLDL + LDL and HDL cholesterol determined several times on each monkey. One of the diet treatments consisted of a combination of oils which had the same fatty acid composition as rice bran oil but did not contain any rice bran oil. From the studies it was concluded that (a) the rice bran oil content of the diet was the primary determinant of the degree of diet-induced hypocholesterolemia, (b) the reductions in serum total and VLDL + LDL cholesterol with rice bran oil feeding were not associated with significant changes in HDL cholesterol, and (c) a component of rice bran oil other than its fatty acid composition was responsible for its hypocholesterolemic action.

In a second study using the same nonhuman primates described above, rice bran oil, corn oil and canola oil fed at 20% of calories (total calories from fat was 30%) when compared to a blend of oils which approximated the average American diet, at 36% calories as fat, all reduced total and VLDL + LDL cholesterol approximately 30%. HDL cholesterol levels were least affected in the rice bran oil group. Thus, despite the high saturated fatty acid and lower polyunsaturated fatty acid profile of rice bran oil compared to the other unsaturated vegetable oils (Table 1), reductions in serum lipoprotein cholesterol levels were comparable, suggesting an important contribution of the non-fatty acid component of rice bran oil to its cholesterol-lowering properties.

The explanation for the hypocholesterolemic action of rice bran oil is unknown but many of its unsaponifiable components have cholesterol-lowering activity due to various mechanisms. For example, plant sterols and triterpene alcohols can inhibit dietary cholesterol absorption and enhance fecal sterol and bile acid secretion. The high content of tocotrienols in rice bran oil (Asaf Qureshi, personal communication) suggests that cholesterol synthesis may be inhibited in individuals fed rice bran oil. Either one of these mechanistic responses can result in the upregulation of the LDL receptor thereby increasing hepatic uptake of circulating LDL and decreasing serum LDL levels. This suggests the possibility of inducing mechanistic synergism in response to the feeding of blends of oils low in saturated and high in unsaturated fatty acids which, when combined with rice bran oil, could alter membrane fluidity and cholesterol absorption and metabolism, and therefore LDL receptor activity. Thus, one might speculate that a blend of the appropriate vegetable oil with rice bran oil would yield a hypocholesterolemic response greater than either oil alone.

Although very preliminary in nature, unpublished studies in humans using rice bran by Gerhardt et al. (38), Nestel et al. (39), and Hegsted et al. (40) have reported reductions in plasma total and LDL cholesterol levels of up to 14%.

In a recent study by Topping et al. (41), it was reported that rice bran compared to wheat bran fed to rats caused significant reductions in plasma cholesterol. Even more interesting was the observation that when rice bran was combined with fish oil (a) the hypotrianglyceremic response of fish oil was enhanced, (b) the activity of hepatic LDL receptor activity was increased relative to wheat bran, and (c) the usual down-regulation of the LDL receptor by fish oil was prevented. The authors speculate that unidentified components of rice bran, possibly in the water-soluble non-starch polysaccharides, are the active ingredients.

The studies reviewed in this communication suggest that the unsaponifiable fraction of various oils can play an important role, alone or in concert with the fatty acid moiety in determining the degree of diet-induced hypocholesterolemia. Much more work needs to be performed in delineating the active components of the unsaponifiable fraction and the subsequent mechanisms of action for each of the fractions. Rice bran oil with its high content of unsaponifiables coupled with the recent demonstration of its hypocholesterolemic properties would seem an ideal candidate for further studies of these interactions. It will be important in the future that well-controlled human studies be performed with rice bran oil incorporated into ordinary foods, at levels which are commonly consumed and compared to dietary oils that normally compose the average American diet.

REFERENCES

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