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Glucomannan minimizes the postprandial insulin surge: a potential adjuvant for hepatothermic therapy

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Summary Glucomannan (GM) is differentiated from other soluble fibers by the extraordinarily high viscosity of GM solutions. Administration of 4–5 g of GM with meals, blended into fluid or mixed with food, can slow carbohydrate absorption and dampen the postprandial insulin response by up to 50%. Controlled clinical studies document that GM can promote satiety and weight loss, lower LDL cholesterol, improve diabetic control, and correct constipation, with minimal if any side-effects. Rodent studies suggest that GM may have potential for decreasing cancer risk and possibly even slowing the ageing process. Hepatothermic therapy, a technique for achieving rapid loss of body fat by optimizing the liver's capacity for fat oxidation, can only achieve its optimal efficacy if diurnal insulin levels are kept low; ingestion of GM with meals will evidently be of benefit in this regard by moderating postprandial insulin surges. © 2002 Published by Elsevier Science Ltd.

GLUCOMANNAN CAN LOWER THE EFFECTIVE GLYCEMIC INDEX OF MEALS

Supplemental soluble fiber, taken with or prior to meals, has potential utility for lowering LDL cholesterol, promoting weight loss, and aiding diabetic control (1–3). Of the many types of soluble fiber that have been tested for these purposes, glucomannan, a slightly branched and lightly acetylated polymer consisting of glucose and mannose (roughly in the ratio of 3 : 5) connected by $\beta 1 \rightarrow 4$ linkages, derived from the traditional Japanese food konjac root, appears to have the greatest practical potential (4–*6*). This reflects the exceptionally high viscosity of solutions of this fiber; 1% solutions of glucomannan (GM) are about 10-fold more viscous than comparable solutions of guar gum, and over a hundred-fold more viscous than pectin solutions (4,*6*). For this reason, relatively modest daily intakes of GM (as low as 4 g per day) can exert worthwhile clinical effects. Garcia and colleagues grasp the implications of their viscosity studies when they conclude that 'glucomannan appears to be the fiber best suited for use as a dietary supplement in the treatment of excess weight, constipation, hyperlipidemia, and diabetes' (*6*). A further advantage is that refined konjac GM preparations (such as Propol^{TM}) are virtually flavorless, and, if stirred briskly into water or juice and consumed quickly, are not associated with an unduly viscous or gritty mouthfeel (5). Fortunately, the viscosity of a newly made 1% solution of GM develops gradually, rising to over 10 000 cps after an hour and reaching a peak at about 5 hours (at least 50 000 cps) (4).

Of particular interest is the fact that, when administered prior to or during meals, pre-solubilized in fluid or pre-mixed with food, GM in doses as low as 4–5 g (approximately one teaspoon) can markedly reduce the effective glycemic index of a meal (4,5,7–*9*). This is associated with a comparable reduction in the postprandial insulin surge. Indeed, two different research groups report that postprandial peak insulin response, as well as area under the insulin curve, can be reduced about 50% by concurrent GM supplementation (4,5). A delay in gastric

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emptying (4), as well as retardation of the degradation and absorption of carbohydrate (5) (and probably protein), appear to account for this phenomenon. Fortunately, although GM slows the absorption of dietary carbohydrate, studies show that it does not induce malabsorption (4), and indeed tolerance to GM in clinical studies has been excellent. (In this respect it contrasts notably with α-glucosidase inhibitors such as acarbose, which commonly induce malabsorption-related side-effects.) Stool volume invariably increases during GM administration (of value to patients who are constipated) (10–12), but there is little if any increase in flatus or other undesirable GI symptoms. In the colon, GM is entirely degraded and metabolized by gut bacteria (13); the increase in stool weight thus reflects an increase in bacterial mass.

The reduction in postprandial glycemia achievable with GM has evident utility in the management of both types of diabetes (9,14–16). Indeed, the first clinical report documenting the use of GM examined its impact on diabetics, and noted that, in type 2 patients, fasting glucose fell by an average of 29%, enabling a reduction or discontinuation of medication in many instances (14). A more recent shorter-term study from the University of Toronto confirms the utility of GM in type 2 diabetes, albeit the reduction in fasting glucose was less dramatic (16). Why *fasting* glucose declines under these circumstances is not entirely clear; perhaps it reflects the fact that postprandial insulin surges down-regulate peripheral insulin receptors (17), a phenomenon that would be minimized during GM administration.

BETTER CONTROL OF APPETITE AND LDL CHOLESTEROL

A portion of the long-term impact of GM on insulin sensitivity might be traceable to a reduction in body weight. Several double-blind studies have concluded that, even when administered in capsules in daily doses as low as 4 g, GM can promote increased weight loss, whether in the context of a hypocaloric diet (18–21) or without a conscious effort at dieting (22). These studies conclude that GM promotes satiety, and that some or all of the bariatric benefit is attributable to decreased caloric intake. A number of factors may contribute to the increased satiety associated with GM administration, including: increased gastric distention and delayed gastric emptying (23), a blunting of the postprandial insulin surge (24), and increased delivery of food to the terminal ileum (where activated chemoreceptors transmit a satiety signal) (25,26).

The ability of GM to decrease serum LDL cholesterol, sometimes quite substantially (by 22% in a recent study with insulin-resistant subjects) (27), has been documented by several studies (22,27,28). In this regard, it should be noted that the recent Harvard meta-analysis examining the ability of supplemental soluble fiber to lower cholesterol levels, which concluded that the achievable benefits were disappointingly small relative to the inconvenience involved, did not include GM studies in their analysis (29). (For reasons unclear to me, American medical scientists have almost totally ignored GM – I could find only one clinical study by American researchers examining the effects of this fiber (22).) Generalizing from studies with other soluble fibers, the reduction in LDL cholesterol is likely to be attributable to increased activity of 7-α-hydroxylase, rate-limiting for the conversion of cholesterol to bile acids (30,31). By decreasing the enteral formation (and possibly enhancing the excretion) of hydrophobic bile acids such as deoxycholate (32), GM should lessen feedback suppression of this enzyme (33). Furthermore, the reduction in postprandial insulin levels achievable with GM would be expected to increase this enzyme's expression (33–35). Increased activity of 7-α-hydroxylase, in turn, would deplete the hepatic cholesterol pool and thus up-regulate expression of the hepatic LDL receptors.

FUTURE PROSPECTS

It has been argued on theoretical grounds that a minimization of diurnal insulin levels could be expected to decrease cancer risk and possibly even slow the ageing process (at least in rodents), owing in part to down-regulation of IGF-I activity (36–38). It is thus of interest to note several reports that GM-rich diets can suppress cancer induction in rodents (39–41). To the extent that systemic IGF-I activity regulates the growth of pre-existing cancer, GM administration might also have some modest utility in cancer treatment. With respect to ageing, Chinese researchers, examining age-related histological changes during long-term feeding of rats with diets that either were or were not enriched with GM, concluded that GM may indeed slow the ageing process (42). If a substantial reduction in diurnal insulin levels is a key mediator of the beneficial effects of caloric restriction (as some believe) (36–38), it is not unreasonable to expect that GM administration could likewise achieve these benefits to some modest degree.

Minimizing diurnal insulin levels – and thus avoiding suppression of the liver's capacity for fatty acid beta-oxidation – is presumably key to the success of hepatothermic therapy (HT) of obesity (43,44), this is why low-glycemic-index foods and low-insulin-response meals are recommended with this regimen. Evidently, administration of GM with meals would be an appropriate adjuvant measure for use with HT, particularly since many patients will be less than totally compliant with food choice recommendations. Furthermore, GM by itself can

promote weight loss – an effect that would likely complement the efficacy of HT in this respect. And when HT is used to manage or reverse type 2 diabetes (45), the utility of GM for minimizing postprandial glycemic excursions would be of evident ancillary benefit. Thus, strong consideration should be given to incorporating GM into the standard HT regimen.

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