Pectin in Health and Disease

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Many higher plants produce economically important organic compounds, such as oil, resins, tannins, natural rubber gums, waxes, dyes, flavors, fragrances, pharmaceuticals, and pesticides. The major groups of secondary metabolites of sugars include cellulose, pectins, starch, gums, and mucilages. These make up dietary fibers, which are basically the skeletal remains of plant cells that are resistant to digestion by enzymes. The particular dietary fiber of interest in my laboratory has been grapefruit pectin. We reported at the First International Symposium on Horticulture and Human Health in 1987 our initial studies, which involved the development of *in vitro* techniques to systematically study dietary grapefruit pectin (Cerda, 1988). We were initially interested in assessing the effectiveness of grapefruit pectin and lowering plasma cholesterol in miniature swine. In this study the effect of grapefruit pectin (*Citrus paradisi*) on plasma cholesterol, triglycerides, and low- and high-density lipoprotein cholesterol was investigated. Miniature pigs were randomized to either 1) controlled diet (hog finisher), 2) a high-cholesterol diet with 3% cellulose, or 3) a high-cholesterol diet with 3% grapefruit pectin. Animals were bled on a monthly basis for the duration of the experiment (326 days). Plasma was assayed for cholesterol and triglycerides and lipoprotein was assayed on the ultracentrifuged fractions. It was concluded that grapefruit pectin significantly lowered plasma cholesterol by nearly 30%, improved the LDLC : HDLC by 31% (compared to a non-pectin high-cholesterol-fed pigs), with no effect on serum triglycerides for the duration of the study. At the end of the feeding experiments, the animals were sacrificed and the effect on grapefruit pectin under development of atherosclerosis was examined. Thoracic and abdominal aorta and the main branches of the coronary arteries were removed. The arteries were prepared and stained for histopathologic evaluation of the severity of atheromatous plaque formation. Although there was some variability, the affected pigs on the pectin-supplemented diet showed an 85% decrease in plaque formation on the surface area of the aortas and an 88% decrease was observed in the narrowing of the coronary arteries. We concluded from these studies, that not only does grapefruit pectin lower plasma cholesterol, but there is a significant reduction of formation of atheromatous plaque in the aorta and coronary vessels. Furthermore, the aforementioned 30% reduction in total plasma cholesterol, with grapefruit pectin-supplemented diet in these miniature swine, was primarily due to a drop in the LDL cholesterol. In this model, grapefruit pectin seemed to be a potent hypercholesterolemia agent. In addition, it appeared that the severity of the atherosclerosis that developed depended on the level of hypercholesterolemia that could be induced, particularly with the most-affected animals on the high-fat cellulose diet. A strong relationship ($R = 0.836$) between percent of surface area with plaque vs. total cholesterol (milligrams/deciliter) for aortas and 0.735 for coronary arteries [percent cross sectional narrowing vs. total cholesterol (milligrams/deciliters)] was observed (Baekey et al., 1988).

We then studied the effect of grapefruit pectin on plasma cholesterol, triglycerides, very-low-density lipoprotein (VLDL), low-den-

sity lipoproteins (LDL), and high-density lipoprotein and the ratio of the LDL to the HDL in a group of subjects with hypercholesterolemia, who were *unable or unwilling* to alter their lifestyle. There were 27 subjects (nine males, 18 females), whose mean baseline plasma cholesterol was 273 mg-dl^{-1} (range of 208 to 420 mg-dl^{-1}). All subjects were healthy volunteers, with ages ranging from 27 to 67 years, for a mean of 59.1 years. They were not on any steroid hormones or medications that could affect or alter the cholesterol levels. All volunteers were screened to be positive for hypercholesterolemia according to the Consensus Conference on Lowering Blood Cholesterol to prevent Heart Disease (American Medical Association, 1985). Volunteers gave their consent to participate in the study, which was approved by the Univ. of Florida Health Center Institutional Review Board and the Clinical Research Advisory Committee. The study was designed to begin with a 4-week baseline of determinations, followed by a 4-week treatment (placebo or pectin), a 4-week period of no treatment and a 4-week treatment period in which the patients were crossed over, with each subject acting as his/her own control. Subjects were instructed to take 27 capsules per day (15 g of pectin) based on 5 g per meal for three meals. If the subjects did not eat three meals a day, they were still required to take the 15 g in three 5-g doses at a "normal" meal time. Encapsulation of pectin and placebo (starch) was coordinated by Pharmacy Services. At no time during the study was the code broken. The subjects were instructed to maintain their normal diet and lifestyle throughout the study and were asked not to change or take any medications without consulting the investigator. Dietary records were kept during the three intervals of the study (weeks 1, 7, and 16). The dietary records were supervised and kept by a dietician. Each subject was instructed to return any unused capsules which were collected and counted for compliance. Other than one patient who complained of an increased number of bowel evacuations (from one to three per day), no side effects were noted. Only two subjects experienced any difficulty in taking this large number of capsules, and this occurred during the initial days of the study. Lipid analyses were performed in our laboratory by standard methods without knowledge as to the status of the patient or the period of the study.

The average percentage of subject compliance was based on the number of capsules returned, divided by the number of capsules dispensed. Subjects when taking pectin had a compliance of 98.4%: when taking a placebo, 98.7%. General protocol compliance was assumed based on the subjects' assurances, as described previously. The mean total plasma cholesterol baseline was 275 mg-dl^{-1} ($\pm 10 \text{ mg-dl}^{-1}$ SEM). When subjects were given the pectin supplement a mean 21 mg-dl^{-1} ($\pm 7.6 \text{ mg-dl}^{-1}$ SEM, ≤ 0.008) resulted. This resulted in a 7.6% decrease in the mean plasma cholesterol level-88.9% of these subjects demonstrated decreases. When subjects were given placebo, cholesterol levels did not vary from the normal baseline of 275 mg-dl^{-1} (11.6 mg-dl^{-1} SEM). No deviation from the baseline occurred, and only 44.4 of the subjects showed any decrease in plasma cholesterol. The HDLC, LDLC, and TG showed no significant decreases in the three groups (baseline, pectin, and placebo). In addition, nine of 27 subjects demonstrated a 10% or greater decrease in cholesterol, 13 demonstrated a 10% decrease in LDLC, and 14 (51.9% of total) demonstrated a reduction in the LDLC : HDLC ratio (Cerda et al., 1989).

It is clear that we now have the ability to bring atherosclerotic cardiovascular disease under control not just by treating symptoms and sequelae, but by actually preventing development and pro-

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gression. The Lipid Research Clinic Coronary Primary Prevention Trial provided definitive evidence that lowering cholesterol reduces coronary heart disease and is, therefore, beneficial. Furthermore, a number of interventional trials have shown that it is possible, either with medication or diet, to reduce the rate of progression of coronary disease by reducing cholesterol (American Medical Association, 1982; Brensike et al., 1984). Not only is the relationship of elevated cholesterol to occurrence and progression of coronary atherosclerosis important, but elevated level of HDLC or reduced levels LDLC may protect against coronary heart disease. Logic dictates the need to lower cholesterol, especially in patients who are at moderate to high risk for coronary artery disease. In these subjects, a change in diet/lifestyle would be advisable. With regard to total population education about eating habits and the relevance of cholesterol levels might gradually achieve a meaningful shift of the whole distribution curve of cholesterol to the left. This could have a great impact on cardiovascular mortality. The 1985 NIH Consensus Development Conference on lowering blood cholesterol to prevent heart disease, had indicated that each 1% reduction of blood cholesterol yields about a 2% reduction in risk for coronary heart disease (American Medical Association, 1985). Our study has shown clearly that a daily dietary supplement of 15 g of grapefruit pectin will significantly lower plasma cholesterol, lower the LDLC, and improve the ratio of LDLC : HDLC in hypercholesterolemic patients who are unable or unwilling to follow a low-risk diet.

We conclude, therefore, that grapefruit pectin, and other food sources rich in pectin, are useful adjuvants to a fat restricted diet in hypercholesterolemic patients. With the recent evidence that from one to four Americans has a cholesterol level that imparts an increased risk of premature coronary heart disease, a broader application in the form of recommendations to include pectin-rich foods and a prudent diet aimed at the primary prevention of atherosclerosis in the general public seems justifiable:

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