EVALUATION OF PUBLICLY AVAILABLE
SCIENTIFIC EVIDENCE REGARDING
CERTAIN NUTRIENT–DISEASE RELATIONSHIPS:

6. DIETARY FIBER AND CARDIOVASCULAR DISEASE

December, 1991
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Bethesda, Maryland 20814
FOREWORD

The Life Sciences Research Office (LSRO), Federation of American Societies for Experimental Biology (FASEB), provides scientific assessments of topics in the biomedical sciences. Reports are based upon literature reviews and the scientific analyses of knowledgeable investigators engaged in work in specific areas of biology and medicine.

This report was developed for the Center for Food Safety and Applied Nutrition, Food and Drug Administration (FDA), in accordance with the provisions of Task Order #9 of Contract No. 223-88-2124. Potential authors and reviewing consultants were identified by the LSRO based on their qualifications, experience, and freedom from conflict of interest, with due consideration for balance and breadth in appropriate disciplines. The author and reviewing consultants were selected with the concurrence of the LSRO Advisory Committee (which consists of representatives of each constituent Society of FASEB).

On March 14, 1991, the FDA requested submission of scientific data and information on the ten specific topics for which health claims might be made (Federal Register 56:12932–12933). The scientific data and information provided in response to this request were considered by LSRO in preparing this report. Copies of the submitted materials are available for public inspection at the Dockets Management Branch, FDA (Docket No. 91N-0099). Copies of documents cited in this report are available for public inspection at LSRO, FASEB.

David Kritchovsky, Ph.D., Associate Director, Wistar Institute, Philadelphia, PA should be cited as the author of this report. The LSRO acknowledges the efforts of David Kritchovsky, Ph.D. and also the critical assistance of Elizabeth L. Barrett-Connor, M.D., Professor of Medicine and Community Medicine, University of California, San Diego, CA; Barbara O. Schneeman, Ph.D., Professor and Chairman, Department of Nutrition, University of California, Davis, CA; and Jon A. Story, Ph.D., Professor, Department of Foods and Nutrition, Purdue University, West Lafayette, IN, who reviewed several drafts of the manuscript. The appendix tables were prepared by the LSRO staff and author and were critically reviewed by the author and reviewers. Subsequently the draft report and tables were revised by the author, edited by the LSRO scientific staff, and received final concurrence from the author and reviewing consultants.

The evaluation of scientific literature, data, and information submitted to the LSRO was made by the author, reviewers, and the LSRO independently of FDA or any other group, governmental or non-governmental. The author and LSRO accept responsibility for the accuracy of the report conclusions and its appendix table(s). This final report was reviewed and approved by members of the LSRO Advisory Committee under authority delegated by the Federation Board. The LSRO Advisory Committee members who reviewed this report were free of conflicts of interest in regard to the subject matter under policies established by the Federation. Upon completion of these review procedures, the report was approved by the Executive Director, FASEB, and transmitted to FDA.

While this is a report of the Federation of American Societies for Experimental Biology, it does not necessarily reflect the opinion of each individual member of the FASEB constituent Societies.

December 31, 1991

Kenneth D. Fisher, Ph.D.
Director
Life Sciences Research Office
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I. INTRODUCTION

A. BACKGROUND INFORMATION

The importance of dietary fiber components in the diet has been recognized for many years but has received increased attention in the past 12 to 15 years. Study of the role of dietary fiber in health and disease was stimulated by the work of Burkitt (1971, 1973a,b) and Painter et al. (1972). These and other investigators hypothesized that the relatively low level of plant fiber in the diets of Western societies predisposed these populations to diseases and disorders which differ in type and severity from those in less developed regions. Interest in this hypothesis has led to a number of laboratory, clinical, and epidemiological studies, suggestions for health benefits of dietary fiber, development of new food products and diets, calls for guidelines on the fiber content and labeling of food products, and revision of nutritional recommendations. However, dietary fiber intake is only one aspect that must be considered in making dietary recommendations and is difficult to address in isolation from the total diet.

Various beneficial health effects have been suggested for dietary fiber, individual components of dietary fiber, and fiber-containing foods. Epidemiological studies and/or clinical trials have been conducted to examine the effects of fiber on glycemic response, lipid metabolism, laxation, diverticular disease, colon cancer, weight loss, and many other conditions. Interpretation of these studies is complicated by differences in the methods used for assessing dietary fiber intake in epidemiological studies and differences in the type and level of fiber components and fiber-containing foods used in clinical trials. The same factors also complicate studies of the potential adverse effects of high amounts of dietary fiber, e.g., altered availability of minerals and trace elements, altered absorption of drugs, changes in bowel function, and others.

1. Definition

Despite increasing public and scientific interest, several problems have impeded research on the health effects of dietary fiber. One major issue has been the absence of a universally accepted definition of dietary fiber. Most definitions encompass a wide variety of compounds with different chemical characteristics and physiological functions.

While the term "crude fiber" has been used for several decades, the definition of "dietary fiber" has been problematical for several years. A classification for dietary products and foods was submitted at the XIII International Congress of Nutrition (Spiller and Jenkins, 1986). Four groupings were presented:

a) Whole foods high in fiber,

b) A high fiber fraction (such as wheat bran) which could be produced without affecting the structure and/or composition of the material as present in the food,

c) Concentrated fibers (isolated polysaccharides) such as pectin or cellulose, which have been altered in the course of extraction from food sources and subsequent purification, and

d) Fiber-enriched foods.
Each of these types of product may contain the same amount of a given fiber, but the action of that fiber will be affected by its physical form and by other substances in the food. For example, is the fiber added to a semi-purified diet the same as that fiber in its natural milieu? Is it the same in steric form? Are its interactions with other dietary components the same?

2. Analysis

As might be expected from the diverse chemical constituents, no one analytical methodology has been entirely satisfactory for identification and characterization of the many components of dietary fiber from all sources.

The analysis of dietary fiber is still not definitive. Marlett (1990) has suggested that the problem has no solution as yet because there are no universally accepted methods of analysis which are based on universally accepted definitions. One major problem lies in the fact that the fiber is an integral part of the foodstuff being analyzed and some of the fiber may be "masked" by its association with other components and nutrients. For example, Marlett et al. (1989) demonstrated that the recovery of soluble fiber is a function of methodology. Thus, pre-treatment with pepsin raises the yield of soluble fiber (percent dry wt of food) by 48 percent in peas, 71 percent in kidney beans, and 15 percent in oat bran.

The designations of dietary fiber as soluble and insoluble fibers are facile but not totally accurate. Almost all fibers occurring in food are a mixture of the insoluble fibers such as cellulose and some hemicelluloses and gelling fibers such as pectin. The soluble fibers (pectin, gums) tend to become viscous in aqueous solution rather than dissolve, as the designation suggests. Thus we are labeling materials by their major component but not total composition, which may be misleading. In general, the brans (wheat, rice, corn, oat) are considered as insoluble fibers but the hypocholesterolemic properties of oat bran are due to its appreciable content of oat gum (β-glucan). An issue that may require more clarification is that food fibers are mixtures whose identities depend in part on analytical methodology used for their identification.

3. Diet–heart disease relationships

The influence of blood cholesterol levels on developing atherosclerosis including coronary heart disease (CHD) has become increasingly recognized as a major risk factor in recent decades. This has led to widespread interest in discovering means of controlling blood cholesterol levels, including dietary intervention. There is some evidence that water–soluble fractions of dietary fiber lower blood cholesterol levels in human subjects (National Research Council [NRC], 1989; U.S. Department of Health and Human Services [USDHHS], 1988), but the significance of the available data in terms of fiber effects has been questioned (Sacks, 1991; Swain et al., 1990).

There is no unequivocal test for the impending coronary attack. Several parameters which are highly correlated with risk have been identified, namely, hypercholesterolemia (or hyperbetalipoproteinemia), elevated blood pressure, and cigarette smoking. However, there are other risk factors which are important but not quite as highly correlated such as, diabetes and obesity. Hopkins and Williams (1981) have identified 246 risk factors; however, most of the studies of the relationship of dietary fiber with CHD have been conducted with one experimental variable, usually, serum cholesterol and the lipoproteins and apoproteins involved in lipid transport. Nevertheless, persons who habitually ingest a high–fiber diet are known to exhibit lower levels of plasminogen activator inhibitor (PAI–1), which leads to increased fibrinolytic activity and reduced risk of thromboembolism (Nilsson et al., 1990).
B. OBJECTIVE AND SCOPE

This review considers the weight of scientific evidence that relates dietary fiber and cardiovascular disease. It reviews and evaluates the literature published since 1987 and compares the conclusions reached with those of previously published exemplary reviews. This report focuses primarily on the influence of dietary fiber on blood lipids but includes brief reviews of hypertension and smoking as additional key risk factors for coronary heart disease.
II. DIETARY FIBER AND CARDIOVASCULAR DISEASE

A. SUMMARY OPINION IN BENCHMARK DOCUMENTS

"The Surgeon General's Report on Nutrition and Health" (USDHHS, 1988) noted an inverse relationship between consumption of vegetable products and CHD mortality, but when analyses of variance controlled separately for the influence of sugar, vegetable products, and fat, sugar and vegetable products no longer were related to CHD mortality. Within-population studies showed lowest serum cholesterol levels in vegans, followed by lacto-ovo-vegetarians, then by omnivores, with highly significant corresponding death rates from CHD. The water-soluble fractions as found in oat bran, guar gum, psyllium seeds, certain beans, and pectin have demonstrated hypocholesterolemic effects in human subjects.

The report "Diet and Health" (NRC, 1989), concluded that in vegetarians, blood levels of total cholesterol, apo-B and apo-A-1 were lower and HDL-cholesterol higher compared with omnivores. The link between fiber and risk of CHD was less consistent than that between fiber and serum lipids. Two studies were cited that suggested a protective effect of fiber against CHD (Khaw and Barrett-Connor, 1987; Morris et al., 1977). The evidence suggested that water-soluble, but not insoluble, dietary fiber lowers serum cholesterol levels.

Animal studies have shown that fiber can influence serum cholesterol levels and atherogenesis; however, these effects vary considerably with the animal model used and the type of fiber added to the diet.

An extensive FASEB review (Pilch, 1987) noted an absence of prospective data on fiber intakes and occurrence of CHD. This review study also noted that the epidemiological data on relationships between dietary fiber and CHD were inconclusive. As in the reports of the Surgeon General and the National Research Council, Pilch (1987) concluded, among other things, that consumption of soluble fibers, particularly guar and oat bran, can have beneficial effects on serum lipid levels in persons with hyperlipidemia.

A prospective study on fiber intake by Khaw and Barrett-Connor (1987) found that fiber intake, as determined at the beginning of a prospective study of heart disease, had a profound influence on outcome. Risk of ischemic heart disease over a 12-year period was reduced significantly in men and women whose early fiber intake was 16 g/d or more. The effect was independent of other dietary variables and other heart disease risk factors.

B. CHOLESTEROLEMIA

In 1980, Kay and Truswell summarized the results of 20 studies involving the effects of wheat bran on serum cholesterol levels. The duration of these studies ranged from several weeks to a year and levels of bran were as high as 72 g/d; however, the results were virtually unanimous in finding no effect. Schneeman and Lefevre (1986) summarized data from 27 studies on effects of fiber on hypercholesterolemia in man and found, generally, that soluble fibers such as pectin or guar gum, as well as other gums, were hypocholesterolemic but most others were without effect. Pilch (1987) reached a similar conclusion. The more recent studies are summarized below (See also Appendix Table).
Whereas earlier studies involved addition of a specific fiber to a prescribed diet, almost all of the newer studies are related to dietary patterns or addition of cereals. For example, Redard et al. (1990) fed adults a high-fiber test meal containing guar gum and oat bran. The investigators observed a postprandial lipemia response in female subjects; however, the responses are not easily interpretable since lipids were measured hourly for seven hours and results presented as percentage change from starting level. Kesäniemi et al. (1990) found that the high-fiber diet increased fecal mass and reduced cholesterol absorption. McIntosh et al. (1991) found barley-containing foods were hypocholesterolemic compared with wheat-containing foods. The barley foods were not active hypocholesterolemic agents when compared with control diet. Psyllium is also known to have hypocholesterolemic effects (Abraham and Metha, 1988; Anderson, 1987; Anderson et al., 1988; Bell et al., 1989; Levin et al., 1990).

Burr et al. (1989) conducted a randomized controlled trial on the effects of dietary advice on myocardial reinfarction in 2033 males under 70 years of age. The diet and reinfarction trial (DART) assessed the effects of dietary advice over a two-year period by monitoring dietary compliance and reoccurrence of ischemic heart disease. Subjects received or did not receive advice on reducing fat intake, increasing intake of fatty fish (mackerel, sardines, salmon, etc.), or increasing cereal fiber intake. All subjects continued to receive antihypertensive, antiangina, anticoagulant, antiplatelet or antiarrhythmic therapy as prescribed by their physicians. Subjects were examined after six months and two years.

After two years, there was no difference in occurrence of deaths from ischemic heart disease between the fat- and no-fat advice groups; however, there were 33 percent fewer deaths from ischemic heart disease in the group advised to eat fatty fish than in the group not receiving this dietary advice (78 vs 116). Deaths from ischemic heart disease were 28 percent higher in the group advised to consume cereal fiber than in the group not so advised (109 vs 85). When compared with their respective control groups, the incidence of all cardiovascular events (fatal and nonfatal) was 8 percent lower in the group advised to reduce fat intake, 15 percent lower in the group advised to eat fatty fish, and 20 percent higher in the group advised to consume cereal fiber. The increase in cereal fiber intake averaged 18 g/d for those receiving the dietary advice versus 9 g/d for the group not receiving the dietary recommendations. The exact nature of the cereal fiber consumed by subjects in both groups was not provided. Burr et al. (1989) noted these observations are at variance with other studies that suggest a benefit from higher fiber consumption. Burr et al. (1989) offered no explanation for the differences other than pointing out that mortality differences in the fiber advice and no-fiber advice groups were not statistically significant.

Resnicow et al. (1991) compared vegans with omnivores and confirmed 9 other studies which found vegans exhibited mean total cholesterol levels approximately 25 percent lower than predicted. Kritchevsky et al. (1984) showed that California Seventh Day Adventist (SDA) vegans have lower cholesterol levels than SDA lacto-ovovegetarians, SDA omnivores, or the general public and that the principal difference in their diet is that SDA vegans ingest more pectin. Percentage fat intake was lowest for female vegans; for male vegans and male and female lacto-ovo vegetarians, fat intake was generally lower than in the other groups except for females in the general population.

C. OTHER RISK FACTORS AND FIBER

1. Hypertension

Elevated blood pressure is also a major risk factor for coronary disease. Dodson et al. (1989) studied 2 groups of 17 subjects. The test group was given a low-fat, high-fiber diet. In this experiment lipid levels were unaffected. Blood pressure fell significantly in the treated group as did body weight, which
might explain the blood pressure findings. Little et al. (1990a,b) fed hypertensive patients diets low in sodium, or low in fat, or high in fiber, or a combination low-fat and sodium, high-fiber diet for 8 weeks. Serum cholesterol levels fell significantly on the low fat or combination diets. The study was confounded because a number of subjects were given diuretics, β-blockers, or both.

2. **Smoking**

Smoking is another major risk factor for coronary disease. Fulton et al. (1988) have found that smokers ingest less fiber than nonsmokers, possibly aggravating risk status. The effects which smoking and/or cessation of smoking have on diet and lipidemia have not been assessed. The general experience is that persons who stop smoking gain weight and thus increase another risk of CHD.

D. **DISCUSSION**

1. **General summary**

Reports during the past four to five years reflect those found in the earlier literature. In general, studies suggested that soluble fiber is hypocholesterolemic while insoluble fiber is not. However, even when foods are used, those rich in β-glucans seem to have more hypocholesterolemic effect (Bell et al., 1990). Fiber is somewhat effective in lowering blood cholesterol even over and above a low-fat diet. The data also indicate an antihypertensive effect of fiber when given as part of a high-fiber, low-fat regimen (Little et al., 1990a,b). The effects of fiber on experimental atherosclerosis were reviewed by Kritchevsky (1986). Although effects vary, depending on the animal model used and type of fiber added to the diet, fiber can influence serum cholesterol levels and atherogenesis in some animal species.

2. **Summary of certain associated factors in the fiber-cardiovascular disease relationship**

a. Basis of association between dietary fiber and cardiovascular disease

The ingredient, dietary fiber, is a food component or may be added to foods. Whether the observed effects result strictly from the fiber or from other components of the fiber-rich food or to a combination of these remains to be determined.

b. Level of intake for a beneficial effect

Blood lipid lowering has been reported for a wide range of experimental intakes from 5.5 g/d to 56 or more g/d, with a rough average of about 30 g/d (9 recent studies). However, there is no agreed upon level of intake for beneficial effects in terms of prevention of coronary heart disease, and some uncertainty, prevails about the true lipid-lowering ability of dietary fiber, especially in normolipidemic subjects. There is no indication of optimum level or even a dose-related effect, as an earlier data compilation also showed (Pilch, 1987). Moreover, whether the effects are the results of fiber per se, accompanying substances, or displacement of fat and/or calories from the diet has not been established with certainty.
c. Optimal level of consumption and duration of effect

There are suggestions as to optimum level of intake for "better health" (e.g. normal bowel function) but not for prevention of disease. The FASEB review (Pilch, 1987) suggested that dietary fiber intake be linked to caloric intake and proposed an intake of 10–13g/1000 kcal.

There are no data relating to transience of fiber effects although this is amenable to experimental testing.

d. Applicability to total U.S. population

Generalization of available scientific information to the entire U.S. population is difficult. Data to support strongly the concept that fiber is protective are insufficient and there are few reports on subjects below 25 and over 65 years old. Presumably persons at high risk such as those with a family history of hyperlipidemia or heart disease would benefit most. Further, it is unclear as to whether the lipid-lowering effects observed in some studies are the result of the fact that most high-fiber diets are low-fat diets.

e. Significant food sources of dietary fiber

Significant dietary sources of fiber (general) are whole grains, legumes, fruits, vegetables, and nuts. In addition, isolated fiber-rich fractions such as wheat and oat bran are added to various foodstuffs and prepared food products.

f. Influence of other dietary, nutritional, or health factors

In a marginally or undernourished population, high fiber intake may lead to trace mineral deficiency. This might also be the case in specific sections of the population (such as the elderly and children) (Pilch, 1987).

g. Safety concerns about reasonable or high levels of consumption

In general, reasonable consumption of a high-fiber diet poses no real health threat and may lead to less calorically dense diets. Sigmoid volvulus and persorption have been reported, but these are rare even in populations ingesting a high-fiber diet. Excessive consumption of fiber supplements is more likely to result in intestinal problems or poor absorption of trace minerals than would be expected from a high-fiber diet.

h. Difference in efficacy among food sources and supplements

Most of the available evidence suggests that isolated polysaccharides such as pectin, guar gum, locust bean gum, oat gum, and psyllium mucilloid have the ability to lower serum cholesterol levels in human subjects. Insoluble fibers such as wheat bran and cellulose are generally ineffective in this respect. There are no data to indicate that a fiber present in a food is the same as when it has been extracted and purified.
i. Critical gaps in knowledge

Questions which have not been answered satisfactorily are:

1) Is the putative beneficial effect a result of fiber or another component of the fiber-rich food? That is, what are the contributions of fiber versus other plant components to lowering serum lipids?

2) If it is fiber, which one(s)? What are the relative contributions of specific categories of fiber types or fiber-rich foods to measurable beneficial effects?

3) Is it higher fiber or lower fat? To what extent can the putative protective effects of fiber be separated from the effects of reduced fat intake?

4) If fiber is shown to be actively protective, what should be the dosage to protect against atherosclerosis and coronary heart disease?

3. Conclusions

Assessing the influences of diets high in fiber on CHD is difficult because such diets are generally lower in fat. Whether the observed effect on cholesterol levels is one of high fiber or low fat is not yet clear, although a few recent studies show that fiber administration following a period on a low-fat (Step I) diet causes a reduction in serum cholesterol values beyond that obtained by diet.

Will fiber prevent heart disease? Some types of fiber affect one of the risk factors (hyperlipidemia) but the definitive evidence that fiber alone can have a significant impact has not been established in replicated trials. In fact the DART study (Burr et al., 1989) suggested that the results may have depended on other dietary factors in addition to fiber. In general, fiber is recommended as part of a dietary life style rather than as a dietary factor possessing pharmacological properties.

Both the Surgeon General’s Report (USDHHS, 1988) and the NRC report (1989) endorsed a dietary pattern higher in grains, fruits and cereals. As part of such a pattern, dietary fiber from certain sources such as barley or oats (Lyon et al., 1987; Van Horn et al., 1991) may be beneficial. This type of advice lacks specificity. The experiments done by Little et al. (1990a,b) show that the low-fat, high-fiber approach helps. Addition of fiber to the diet after cholesterol reduction will lead to another increment of lipid reduction.

The data suggest that diets high in fiber-rich foods can influence lipidemia, but this effect is probably due to overall changes in the diet caused by the addition of fiber sources rather than to simply a direct effect of fiber.
III. BIBLIOGRAPHY


*This bibliography contains all reference citations that are either in the text or the appendix table, or both.


APPENDIX

CRITERIA FOR INCLUSION OF ARTICLES IN APPENDIX TABLE

Articles in peer-reviewed journals related to the topic of this review were selected primarily on the basis of date and content. In general, papers appearing in 1987 or thereafter were included, provided that they presented original data from studies in humans. Certain items tabulated for the sake of completeness may not have been cited in the body of the text if their weight or relevance did not add significantly to development of the author's argument. Reviews have not been listed except as they included new data or useful meta-analyses.
# APPENDIX TABLE 1: STUDIES OF THE EFFECTS OF DIETARY FIBER ON RISK OF CARDIOVASCULAR DISEASE IN HUMAN SUBJECTS

<table>
<thead>
<tr>
<th>Reference</th>
<th>Study Design</th>
<th>Number and Description of Subjects</th>
<th>Duration of Study</th>
<th>Source and Identity of Test Material</th>
<th>Dosage of Test Material</th>
<th>Base Diet</th>
<th>Additional Treatments</th>
<th>Other Factors Affecting Data Interpretation</th>
<th>Results</th>
<th>Assessment of Study</th>
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</thead>
<tbody>
<tr>
<td>Abraham and Mehta, 1988</td>
<td>Dietary intervention</td>
<td>7 healthy ♀ with plasma chol &lt;250 mg/dL</td>
<td>3 wk suppl. period</td>
<td>Ground pythium buck</td>
<td>21g/d</td>
<td>Controlled and uniform</td>
<td>8-d feces collections for steroids; retinol added to meals for retinyl esters</td>
<td>T-chol, LDL-chol, HDL-chol decreased (p&lt;0.002, p&lt;0.01, p&lt;0.03 respectively)</td>
<td>A careful study of pythium mechanisms</td>
<td></td>
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| Anderson et al., 1988 | Clinical trial Dietary intervention: C, D, P, F, and serum lipids | 25♂ 30–65 yr with serum chol between 4.78 and 8.28 mmol/L (185 and 320 mg/dL) | 10 wk (including 2 wk. baseline period) | Metamucil® (79% pythium hydrophilic muciloid) or placebo (inert cellulose fiber) | 3.4 g t.i.d. at meal times | Usual diet (<300 mg chol/d, 20% energy from P, 46% from CHO, 40% from P) | Customary medications for subjects with mild hypertension, arthritis, angina, anxiety, stomach discomfort; aspirin for heart attack prophylaxis | N=14 for treated group and for placebo group | 14.8%; 20.2%; 14.8% ↓ in serum total chol, LDL-chol, and LDL/HDL respectively after 8-wk treatment with pythium | Valuable contribution More studies are needed, with larger N and longer duration. |

| Anderson and Siesel, 1990 | Clinical trial Dietary intervention: B, serum lipoproteins/ast and wheat bran | 25♂ 38–73 yr serum chol, 192–224 mg/dL. | 4 wk (including 1 wk control diet) | 30 g/d fiber from oat or wheat bran (12 and 5 g soluble fiber respectively) | Commonly available foods providing 43% CHO, 16% P, 41% F, 450 mg chol | N=10 for each treated group | Short duration | Oat Bran: 13%, 15%, 15% ↓ in serum total chol, LDL-chol and apo B-100 respectively Wheat bran: slight in above measures as well as in apo A-1 and TGs | Useful contribution to definition of effects of oat and wheat bran |

| Anderson et al., 1990a | Clinical trial Dietary intervention: serum lipoprotein diets | 25♂ 37–69 yr with hyperlipidemia, initial serum chol 5.16–10.91 mmol/L, serum TG 0.93–9.39 mmol/L, 24 completed the study | 28 d (including 7d control diet) | Campbell’s canned pork and beans | Group A—120g beans, single dose Group B—120g beans divided in 2 meals Group C—100g beans at lunch, 62g beans at dinner | Resemblance typical American diet: 42% energy as CHO; 16% as P, 38% F, and 420 mg chol | A metabolic ward study Relatively short-term | All diets combined lowered serum chol and triglyceride 10.4% and 10.8% respectively. Diets B and C were equally effective, and lowered serum chol more than diet A. | Useful contribution Well designed and executed All decreases significant |

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1 The references cited in this table refer to the text or this table or both.
## APPENDIX TABLE. STUDIES OF THE EFFECTS OF DIETARY FIBER ON RISK OF CARDIOVASCULAR DISEASE IN HUMAN SUBJECTS

<table>
<thead>
<tr>
<th>Reference</th>
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<th>Duration of Study</th>
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<th>Dosage of Test Material</th>
<th>Base Diet</th>
<th>Additional Treatments</th>
<th>Other Factors Affecting Data Interpretation</th>
<th>Results</th>
<th>Assessment of Study</th>
</tr>
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<tbody>
<tr>
<td>Anderson et al., 1990b</td>
<td>Dietary intervention trial of effects of oat bran cereal on serum lipid concentrations; R, C, crossover design</td>
<td>14+ with 1 serum chol and TG (5.43–8.43 mmol/L and 1.23–3.69 mmol/L respectively)</td>
<td>4 wk</td>
<td>Oat bran cereal from commercial source Control: generic corn flakes</td>
<td>21 g fiber/d</td>
<td>Similar to typical U.S. diet, 43% energy from CHO, 16% from P, 41% from CHO, 335 mg chol/d</td>
<td></td>
<td></td>
<td>Oat bran: total chol 6.4% LDL-chol 8.2% HDL-chol 1.3%</td>
<td>Oat bran effective in hyperlipidemic subjects</td>
</tr>
<tr>
<td>Behall, 1990</td>
<td>Study #1. Clinical trial Dietary intervention: serum lipids 4 fibers (6 diets in random rotation pattern)</td>
<td>12 yr Ages and other characteristics ND</td>
<td>20 wk</td>
<td>4 refined fibers: cellulose, carboxymethyl cellulose gum, locust bean gum, karaya gum 5 diets – basal alone and basal plus each fiber</td>
<td>7.6 oz. refined fiber/1000 kcal basal diet</td>
<td>14.5% of energy from P, 35% of CHO, 60% from CHO</td>
<td></td>
<td></td>
<td>Data presented in this paper included material published between 1984 and 1989 from Behall and colleagues.</td>
<td>Useful contribution to relatively short-term database</td>
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<td></td>
<td>Study #2. Clinical trial Dietary intervention: serum lipoprotein/guar gum</td>
<td>7 yr, 9 yr with non-insulin dependent diabetes</td>
<td>6 mo</td>
<td>High–CHO–guar gum food bar or food bar without guar</td>
<td></td>
<td>Basal diet + guar gum food bars: 55% CHO; 16% P, 31% F</td>
<td></td>
<td></td>
<td>Serum chol 10–16% lower after gums Effects of gums on LDL-chol similar to total chol but no effect on VLDL or HDL</td>
<td>Important result: lack of hypolipidemic effect of guar in long-term supplement use</td>
</tr>
<tr>
<td>Bell et al., 1990</td>
<td>Clinical trial Dietary intervention: R, DB, PC; on ability of soluble dietary fiber to lower serum chol</td>
<td>68 yr patients with mild to moderate hypercholesterolemia, age 24–69 yr</td>
<td>12 wk</td>
<td>Control cereal: corn flakes Pectin–enriched cereal: oat bran, sugar beet fiber, white wheat bran high–methoxy Pectin Poyllium–enriched cereal: oat bran, sugar beet fiber, white wheat bran, and poyllium</td>
<td>Proportions of total dietary fiber as soluble fiber: corn flakes=0 % Pectin-enriched = 10.76% Poyllium-enriched = 10.20%</td>
<td>Step 1 diet = 6 wk (30% energy as F, 55% as CHO, 16% as P, &lt;300 mg chol) Test diet: step 1 diet plus control supplement (corn flakes) or pectin or poyllium-enriched supplement</td>
<td></td>
<td></td>
<td>Eligibility criteria screened out patients with significant metabolic, cardiovascular, hepatic, renal, or gastrointestinal disorders</td>
<td>Only poyllium significant after Step 1 diet</td>
</tr>
</tbody>
</table>
## APPENDIX TABLE: STUDIES OF THE EFFECTS OF DIETARY FIBER ON RISK OF CARDIOVASCULAR DISEASE IN HUMAN SUBJECTS

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<tr>
<td>Burr et al., 1989</td>
<td>Clinical trial: Dietary intervention; R, C, on effects of diet on secondary prevention of myocardial infarction (MI)</td>
<td>2 yr</td>
<td>Three dietary interventions were used: reduced fat intake with increased PUFA − SFA ratio, increase in fatty fish intake, increase in cereal fiber intake.</td>
<td>Increased intake of cereal fiber to 18 g/d compared with 9 g/d in pts not given fiber advice</td>
<td>ND</td>
<td></td>
<td>Compliance difficulties; some controls shifted to an intervention diet.</td>
<td>No evidence of any benefit in 2-yr all-cause mortality No significant changes in serum chol in the fiber group</td>
<td>Validity of data in question because of methodologies imposed in such a large study. Not applicable to a healthy population</td>
</tr>
<tr>
<td>Davidson et al., 1991</td>
<td>Clinical trial: Dietary intervention; CSR, on hypocholesterolemic effect of 8-gluca</td>
<td>12 wk (included 6 wk treatment period then a 6 wk washout period)</td>
<td>Commonly available oatmeal, oat bran, and fatina</td>
<td>Fat-modified diet within 3 points of NCEP step 1 diet</td>
<td>Oatmeal or oat bran: 28, 66, 84 g/d; fatina: 28 g/d; 7 randomized treatment groups</td>
<td>1 LDL-chol: 10% with 84 g oatmeal 15.9% with 56 g oat bran 11.5% with 84 g oat bran</td>
<td>Data suggest the higher 8-gluca content of oat bran accounts for greater LDL-chol</td>
<td>8-ss</td>
<td></td>
</tr>
<tr>
<td>Demark-Wahnefried et al., 1990</td>
<td>Dietary intervention trial of fat-modified or oat bran-supplemented diets and serum chol P, R, UC</td>
<td>12 wk</td>
<td>Oat bran (OB) from a major food manufacturer</td>
<td>Usual self-selected diet</td>
<td>4 diet groups: Low-fat, low-chol (LFLC); Low-fat, low-chol plus 60 g/d OB (LFLC+OB); 50 g/d OB (OB); 42.5 g/d OB cereal with 8-gluca (POB)</td>
<td>There was no independent control group. Substantial number of subjects did not respond to diet therapy.</td>
<td>Total serum chol decreases: LFLC = 17.1%; LFLC+OB = 13.1%; OB = 12.3%; POB = 10.1%. No difference between groups. However there were non-responders in each group. All groups except POB had 1 HDL-chol.</td>
<td>Lack of control group and limited sample size require caution in interpreting the data.</td>
<td></td>
</tr>
<tr>
<td>Dodson et al., 1989</td>
<td>Dietary intervention trial of high-fiber, low-fat, low-sodium diet on hypertension R, B, C</td>
<td>3 mo</td>
<td>Readily available foods</td>
<td>High-fiber 40−50 g/d intended; sodium 69−80 mmol/d; fat (% energy)−25</td>
<td>Modern western diet (UK) for controls</td>
<td>Compliance with the modified dietary regimen was not optimal and DF intake did not change from pretest values (19.3 to 21 g/d)</td>
<td>Mean systolic and diastolic pressures: 17.8 mm Hg and 12.4 mm Hg respectively; weight loss and urinary sodium output changes significant in diet intervention group. No change in serum lipids</td>
<td>Failed to show a fiber effect</td>
<td></td>
</tr>
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## Appenix Table. Studies of the Effects of Dietary Fiber on Risk of Cardiovascular Disease in Human Subjects

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<tr>
<td>Glassman et al., 1990</td>
<td>Clinical dietary intervention using saturated fat-restricted and soluble fiber-supplemented diet</td>
<td>36 children 22♂, 14♀ with Type IIa hyperlipidemia Age 3-77; 2 = (0.74± 0.72)</td>
<td>8.1± 2.4 mo</td>
<td>Psyllium; source ND</td>
<td>Psyllium supplement twice daily (&lt; 7 yr = 2.5g; &gt; 7 yr = 10g)</td>
<td>10% total calories as sat. fat</td>
<td></td>
<td></td>
<td>The 10% sat. fat diet with soluble fiber supplement yielded reductions of 18% and 23% in total and LDL-chol respectively.</td>
<td>Study documents effects of reduction of sat. fat intake and psyllium-soluble fiber intake in childhood Type IIa Hyperlipidemia</td>
</tr>
<tr>
<td>Kesseli et al., 1990</td>
<td>CO trial of high---and low-fiber diets on chol metabolism P, R, SC</td>
<td>34♂ patient volunteers 47-55 yr</td>
<td>8 wk low-fiber</td>
<td>Fruits, veg, salads, berries, hot porridge with oat flakes, bran, guar gum and pectin</td>
<td>High-fiber 26.2 g/d</td>
<td>Usual diet</td>
<td></td>
<td>There was no ‘washout’ period at crossover</td>
<td>High-fiber diet: slight but significant 1 in total chol (-4.5%); LDL-chol (-6.9%); HDL-chol (-5.7%).</td>
<td>The high-fiber diet was associated with slight 1 of total energy, CHO, and P intakes whose possible influence on serum lipids was not explained.</td>
</tr>
<tr>
<td>Lampe et al., 1991</td>
<td>CO trial of effects of controlled formula fiber diets on blood lipids and fecal bile acid excretion, P, R, SC</td>
<td>18♂, 16♀ healthy volunteers, 19-50 yr</td>
<td>3 wk each of 6 diets</td>
<td>Diets: fiber-free, 10g WB, 30g WB, 10g VF, 30g VF, 30g SBF</td>
<td>See preceding column</td>
<td>A nutritionally adequate liquid formula whose percentage energy from fat was between 35.2 and 37.4.</td>
<td></td>
<td>Although described as healthy, 6 subjects had marginal blood lipid levels</td>
<td>Serum chol decreased significantly with 30g VF and 30g SBF. Reduction of chol by SBF resulted largely from the LDL-chol fraction.</td>
<td>Supports concept that soluble DFs are more hypocholesterolemic than non-soluble DFs in subjects consuming high-fat controlled diets</td>
</tr>
<tr>
<td>McIntosh et al., 1991</td>
<td>CO trial of barley and wheat F on plasma chol in mildly hypercholesterolemic ♂ (range 5.4-7.0 mmol/L), P, R, SC</td>
<td>21♂, 30-59 yr</td>
<td>4 wk each of 2 diets</td>
<td>Barley foods and wheat foods</td>
<td>TDF 38.4 g/d</td>
<td>2182 kcal (P=16.5%; CHO 49.5%)</td>
<td></td>
<td>Weighed food intakes recorded every 3 d throughout 11 wk; 8 fasting blood samples</td>
<td>Barley foods associated with 6% (p&lt;0.05) fall in plasma total chol and 7% (P&lt;0.02) in LDL-chol, compared with wheat</td>
<td>High quality study</td>
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# APPENDIX TABLE. STUDIES OF THE EFFECTS OF DIETARY FIBER ON RISK OF CARDIOVASCULAR DISEASE IN HUMAN SUBJECTS

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<tr>
<td>Miettinen and Tarplia, 1989</td>
<td>Clinical trial, crossover 9 hyperlipidemic subjects 8 subjects with symptomatic diverticulosis</td>
<td>Pseudium seed hydrophilic mucilloid; 9 age-matched subjects, 42% 4 yr; sex ND; 1 with Type IIb 8 with Type IIIA hyperlipidemia</td>
<td>ND</td>
<td>Vi-Solin®</td>
<td>30g/d</td>
<td>Low-chol diet 110 mg/2400 kcal 15 g/d fiber</td>
<td>Duration of experiment was not specified, but was noted as &quot;short-term&quot;</td>
<td>LDL-chol ↓</td>
<td>Confirm role of viscous soluble fibers on LDL-chol, fecal elimination of chol, and increased chol synthesis</td>
<td></td>
</tr>
<tr>
<td>Newman et al., 1989</td>
<td>Dietary intervention trial</td>
<td>14 healthy 9 aged 35 yr &amp; older</td>
<td>4 wk</td>
<td>Wheat flour plus wheat bran; barley flour milled by authors</td>
<td>75% wheat/25% wheat bran or 100% barley flour @ 14g t.i.d. = 42g/d</td>
<td>All cereal containing foods with 75/25 wheat bran or 100% barley flour</td>
<td>No lipid-lowering medications</td>
<td>Subjects on weight reduction diets</td>
<td>Wheat subjects T-chol &amp; LDL-chol ↓; barley subjects if normal at start-no change; if high at start T-chol &amp; LDL-chol ↓</td>
<td>No subjects limited Duration short Results consistent with other studies</td>
</tr>
<tr>
<td>Redard et al., 1990</td>
<td>CO trial of the effect of guar gum and oat bran on postprandial glycemia, lipemia, and lipoprotein composition F, SC</td>
<td>6 6 9 healthy volunteers, 27 yr (4) and 29 yr (4)</td>
<td>1 day for each test meal</td>
<td>Low-fiber meal: farina High-fiber meal: oat bran and guar gum</td>
<td>Low-fiber meal-0.4g High-fiber meal-1.6g for φ, 12 g for 7.</td>
<td>42% of energy as CHO, 16% as P, 42% as F</td>
<td>φ-no effect on postprandial triglyceridemia ↓ postprandial triglyceridemia greater with high-fiber meal</td>
<td>Incorporation of guar gum and oat bran into a test meal alters postprandial lipemia response and there is a gender influence.</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Resnicow et al., 1991</td>
<td>Analysis of serum lipids and diet in vegan vegetarians</td>
<td>31 volunteers (17 9 14 4) 5–45 yr, of which 8 were children 8 thru 17 yr and 22 adults 19 thru 46 yr Controls: 30 age-, sex-, and race-matched volunteers</td>
<td>No food of animal origin for 8 no preceding blood samples</td>
<td>Pure vegetarian diet</td>
<td>Vegetarian diet</td>
<td></td>
<td>Compare with omnivores</td>
<td>Total chol 24% lower than in omnivores</td>
<td>Careful study Confirms previous data</td>
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<td>Superko et al., 1988</td>
<td>Single blind random crossover; 6 groups</td>
<td>44 healthy 60 age 51 ± 12 yr</td>
<td>8 wk</td>
<td>Guar gum liquid medium viscosity (DYCOL 4500°F) high viscosity (HENKEL 6214)</td>
<td>15 g/d</td>
<td>Customary medication and anti-hypertensives</td>
<td>Antilipemics withdrawn 4 wk before trial; flatulence &amp; loose stools; HDL chol n=16 placebo group C.</td>
<td>Subjects preferred liquid formulation. Total chol &amp; LDL chol reduced with guar gum therapy TO, HDL chol no change; total and LDL chol returned toward baseline at 8 wk</td>
<td>Variability of results in placebo group C affected statistical power. Viscosity of guar preparation appears important.</td>
<td></td>
</tr>
<tr>
<td>Swain et al., 1990</td>
<td>Dietary intervention: crossover, R, DB, of effect of oat bran on serum lipids and blood pressure</td>
<td>20 healthy volunteers (45, 16 f) mean age 30 yr</td>
<td>15 wk</td>
<td>Oat bran or refined low-fiber wheat from commonly available sources, used in muffins or entrees</td>
<td>Total DF: High-fiber 38.9 g/d Low-fiber 18.4 g/d</td>
<td>Usual self-selected diet</td>
<td>Baseline diet: 2065 kcal, 30.6% fat</td>
<td>Both supplemented lowered mean baseline serum chol by 7 to 8%. Oat bran lowered LDL chol/HDL chol by 9%. Low fiber diet did not change ratio. Oat bran did not significantly lower serum chol any more than refined low-fiber wheat.</td>
<td>Oat bran appears to have little chol lowering action in subjects with normal serum chol levels.</td>
<td></td>
</tr>
<tr>
<td>Tuomilehto et al., 1988</td>
<td>Prospective dietary intervention study of the effect of guar gum on hypercholesterolemia</td>
<td>23 hypercholesterolemic pts (9 m, 14 f) 37-67 yr</td>
<td>1 yr</td>
<td>Granulated guar gum from commercial source</td>
<td>Increased by steps from 7.5 to 30 g/d for 11 subjects; 15-25 g/d for 12 subjects</td>
<td>Usual diet</td>
<td>Diminishing dietary compliance, gastrointestinal side effects</td>
<td>Serum total chol 1 from 10 to 8.2 mmol/L after 8 wk and to 9 mmol/L after 60 wk LDL chol 1 15% after 34 wk and apo B 1 14%.</td>
<td>Effective, but attenuates with time.</td>
<td></td>
</tr>
<tr>
<td>Van Horn et al., 1991</td>
<td>Dietary intervention study of effect of instant oats on serum lipids in hypercholesterolemic subjects</td>
<td>42 hyperlipidemic subjects (21m, 21 f) 25-76 yr Controls: 38 hyperlipidemic subjects (19 m, 19 f) 22-69 yr</td>
<td>8 wk</td>
<td>Instant oats 56.7 g/d of oats (5.6 g DF/d)</td>
<td>Usual diet except intervention group substituted oats for other CHO in their diets.</td>
<td>Total cholesterol: Oats = 6.3% Control = 1.4% LDL chol 1: Oats = 9.2% Control = 3.7%</td>
<td>Careful study Confirms data from some other studies</td>
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**Key**
- C=Controlled
- CHO=Carbohydrate
- R=Randomized
- LDL chol=LDL Cholesterol
- DB=Double Blind
- F=Fat
- FC=Placebo controlled
- TG=Triglyceride
- apo B=apolipoprotein B
- ND=not described
- UC=Uncontrolled
- VF=Vegetable Fiber
- WF=Wheat Fiber
- SHF=Sugar Beet Fiber