Reyna-Villasmi, Nadia; Bermúdez-Pirela, Valmore; Mengual-Moreno, Edgardo; Arias, Nelly; Cano-Ponce, Clímaco; Leal-Gonzalez, Ellizu; Souki, Aida; Inglett, George E.

Oat derived-glucan significantly improves HDLc and diminishes LDLc and Non-HDL cholesterol in overweigh individuals with mild hypercholesterolemia

Revista Latinoamericana de Hipertensión, vol. 1, núm. 3, julio-septiembre, 2006, pp. 28-34

Sociedad Latinoamericana de Hipertensión
Caracas, Organismo Internacional

Available in: http://www.redalyc.org/articulo.oa?id=170217081004
Objective: To investigate the effect of bread formulated with 6 g. β-glucan in normotensive subjects with overweight and mild-to-moderate hypercholesterolemia.

Design: The 38 eligible patients ate an isocaloric diet for 1-week period; they were divided in two groups. Group A was treated with step II American Heart Association (AHA) diet and Group B, treated with AHA step II diet plus bread containing β-glucan for 8 weeks. Plasma lipids were measured during baseline and after weeks 8 in all patients.

Results: There was a significant increase in plasma HDLc in the oat β-glucan group from 38.9±1.9 to 48.8±2.1mg/dl; p<0.001, while B group remained without change. Oat β-glucan consumption significantly reduced plasma total cholesterol and LDLc from 231.5±4.0 to 195.2±4.1md/dl and 167.6±4.0 to 122.2±3.5md/dl (p<0.001) respectively. Both diets showed a significantly drop in total cholesterol and LDL-c total cholesterol and LDLc with no significant differences between treatments. In the β-glucan diet, TC-LDL/HDLc ratios showed significant decreases when compared with the AHA diet. Oat β-glucan consumption diminished significantly non-HDL cholesterol compared with the AHA diet p<0.04.

Conclusions: Six grams β-glucan (Nutrim-OB) from oat administered in bread added to AHA diet and exercise can reduce lipidic risk factors associated with CVD in overweight and mild hypercholesterolemic male subjects.

Key Words: β-glucan, oat soluble fiber, HDL cholesterol, LDL cholesterol, Non-HDL cholesterol.

Introduction

n, 1963, De Groot et al1 were the first report that the addition of an oat product to the diet of human lowered blood cholesterol concentrations. Since the report, many animal and human studies have investigated the beneficial effects attributed to the ingestion of oat products, including improvements in gastrointestinal function, modulation of glucose metabolism, and decreased blood cholesterol concentration2,3.

Oats, an important source of water-soluble fiber, have long been reorganized as a potential cholesterol-lowering dietary component. In January 1997, the US Food and Drug Administration passed a unique ruling that allowed oat brand to be registered as the first cholesterol-reducing food, with a recommended dosage of 3 g β-glucans incorporated into a palatable cereal product4.

A diet high in fiber has been linked to a decreased risk of mortality from cardiovascular disease (CVD), independent of energy intake, dietary fat intake, and other dietary factors5. Meta-analyses have shown that the consumption of soluble fiber, such as β-glucans in oat products, reduces blood total-cholesterol and LDL-cholesterol concentrations6,7. Thus, the ability of soluble fiber to reduce CVD risk is in part related to its ability to favorably modify blood lipids and lipoproteins.
The importance of decreasing low-density lipoprotein cholesterol (LDLc) levels for CVD prevention has been well recognized in clinical trials8,9. The risk of nonfatal myocardial infarction (MI) and coronary death was reduced by 20%-40% following treatment with LDLc-lowering drugs10,12.

The importance of low HDLc levels (40 mg/dl) as a risk factor for the development of CVD is recognised by current British, European and US guidelines13, although a target for raising HDLc is not specified. The National Cholesterol Expert Panel guidelines14 (NCEP ATP III) has placed a greater emphasis on low HDLc levels and has revised the level below which HDLc is considered to be a CVD risk factor from 35 mg/dl to 40 mg/dl. Furthermore, the guidelines recommend the use of drugs for raising HDLc in individuals with isolated low HDLc levels and CVD or CVD risk equivalents14.

No specific treatment goals are defined for HDL cholesterol and triglycerides, but the lipidic fractions are used as markers of increased risk and should also be used to guide the choice of drug therapy1. Current lipid-modifying therapies that raise HDLc concentration include bile acid binding resins, fibrates, nicotinic acid and statins14,20. Niacin21,25 raises HDLc levels by up to 30%, and increases of 10%-15% have been reported with fibrates22,23. Statins and well tolerated, effective LDLc-lowering drugs with beneficial effects upon HDLc23,28. However, long term effects of chronic use of these drugs in dyslipidaemic patients should be considered, especially taking into account post-marketing toxicity reports about some statins and combined therapy with fibrates.

The aim of the study was to investigate the effect of bread formulated with 6 g. β-glucan in normotensive subjects with overweight and mild-to moderate hypercholesterolemia.

Subjects
A total of 38 mildly hypercholesterolemic male subjects [total cholesterol: 200-240 mg/dl (5,18 - 6,2 mmol/L)] patients with body mass index (in Kg/m²) between 25-30 were recruited from an over weigh population consulting at the Center for Endocrine and Metabolic Research (CIEM), The University of Zulia, Maracaibo-Venezuela. At entry, subjects ranked between 55 and 72 years (Mean 59,84 ± 0,61 years), with a mean BMI of 28,30 ± 0,56 Kg/m², mean plasma total cholesterol of 232,3 ± 2,4 mg/dL and HDLc of 40,73 ± 1,62 mg/dL. Individuals were excluded if they reported or were observed to have CVD, to have self-reported diabetes or a fasting blood glucose concentration >7,0 mmol/L, to be a systolic blood pressure >140 mm Hg or a diastolic blood pressure >90 mm Hg, to have tobacco use, to have a history of eating disorders or of thyroid gland disorders, or renal disease or to use any medications known to affect any of the dependent variables in the study. The research protocol was approved by the bioethics committee of CIEM. All subjects provided written, informed consent before participation.

Study design and measurements
The subjects were selected and well motivated. All eligible participants were committed to take an isocaloric diet for one week (wash out period). After 12-hours, fasting venous blood sample was drawn in order to measure total Cholesterol, triglycerides and HDLc by an enzymatic method (Human GmbH, Germany). LDL cholesterol (mg/dl) and VLDLc were calculated by Friedewald’s formula13 and Non-HDLc was calculated by addition of LDLc and VLDLc24. After adaptation during this period, subjects were randomly assigned to one of two interventional groups: A control group (n=19): American Heart Association (AHA) Step II diet11, plus whole wheaat bread as main fiber 6 g/day and walking 60 minutes/day or B experimental group (n=19): AHA Step II diet, walking 60 minutes/day plus bread containing soluble fiber 6 g/day (Nutrim-OB, provided by USDA-ARS Cereal Products and Food Science Research Unit, Peoria, USA). β-glucan and whole-wheat bread Composition was not significantly different (Table 1). Subjects returned weekly for 8 weeks to be weighed and to obtain more bread. A combination of change in body weight and reported physical activity were under supervision at the Nutrition Unit. Finally, at week 8, 12-hours fasting concentrations of all parameters described above were assessed again.

The American Heart Association dietary guidelines for healthy American Adults recommend a diet that provides <10% of calories from SFA, up to 10% from PUFA, and as much as 15% from MUFA. The recommendation to limit total dietary fat to 30% of calories is intended to facilitate the reduction of SFA and to help control calories to manage weight in the group B, the MUFA were provided in 20%.

To evaluate the organoleptic properties of both, was used a test of qualification29, which each subject completed questionnaires designed to rank acceptability, evaluating appearance, colour, aroma, texture and flavour that were rated on a scale of 0 to 9, with 0 being the worst attribute and 9 the best one30.
Statistical analyses

Data are presented as means ± EE, except for satiety, tolerance, and acceptability, which are presented as medians. Treatment effectiveness is also presented as increment or diminution percentages. Paired student t test was used to compare means before and after treatment in each group. One tailed t test was used to compare percentage increments or decreases after treatment between both interventional groups. Mann and Whitney U was used to assess differences between whole wheat bread and β-glucan bread on acceptability variables. All statistical procedures were performed with SPSS version 11.01 and differences with a value of p<0.05 were considered significant.

Body weigh and BMI behaviour

As noted above, a total of 38 subjects completed the study. Subjects were middle to old-aged (59.84 ± 0.61 years) and overweight according to body mass index (in kg/m²; 28.30 ± 0.56). Baseline energy intake (isocaloric diet) was 2582 ± 250 Kcal/day and energy intake during β-glucan diet or AHA Step II diet was 2254 ± 220 Kcal/day and 2265 ± 250 Kcal/day respectively with no significantly differences found between them.

All patients experienced a significant weight loss. However, group B had a better response from 76.8±2.6 at baseline to 71.0±2.4 Kg post-treatment (IMC: 28.4±0.8 to 26.2±0.8 Kg/m²) Vs. only 76.0±2.2 to 72.2±2.3 Kg (IMC: 28.2±0.8 to 26.8±0.8 Kg/m²) in group A, p<0.002. Table 2.

Table 1. β-glucan and whole-wheat bread Composition

<table>
<thead>
<tr>
<th></th>
<th>Whole-wheat bread per each 100 gr.</th>
<th>β-glucan bread per each 100 gr.</th>
</tr>
</thead>
<tbody>
<tr>
<td>Energy (Kcal)</td>
<td>306.5</td>
<td>244.6</td>
</tr>
<tr>
<td>Protein (gr)</td>
<td>9.35</td>
<td>9.64</td>
</tr>
<tr>
<td>Fat (gr)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Total</td>
<td>5.98</td>
<td>1.47</td>
</tr>
<tr>
<td>SFAs</td>
<td></td>
<td></td>
</tr>
<tr>
<td>MUFA's</td>
<td></td>
<td></td>
</tr>
<tr>
<td>PUFAs</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Carbohydrates (gr)</td>
<td>52.9</td>
<td>48.2</td>
</tr>
<tr>
<td>Dietary fiber (gr)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Total</td>
<td>2.1</td>
<td>8.68</td>
</tr>
<tr>
<td>Soluble (β-glucan)</td>
<td>0.37</td>
<td>6.14</td>
</tr>
<tr>
<td>Insoluble</td>
<td>1.73</td>
<td>2.54</td>
</tr>
</tbody>
</table>

SFA, saturated fatty acid; MUFA, monounsaturated fatty acid; PUFA, polyunsaturated fatty acid

Table 2. Body weight, fasting plasma glucose and lipid profile in group A (AHA diet alone) and group B (AHA diet plus β-glucan supplementation)

<table>
<thead>
<tr>
<th></th>
<th>Group A (n=19)</th>
<th>Group B (n=19)</th>
<th>Mean treatment difference (%)*</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Baseline</td>
<td>After treatment</td>
<td>p</td>
</tr>
<tr>
<td>Body weight (Kgs.)</td>
<td>76.0 ± 2.2</td>
<td>72.2 ± 2.3</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Body Mass Index (Kg/m²)</td>
<td>28.2 ± 0.8</td>
<td>26.8 ± 0.8</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Fasting Plasma Glucose (mg/dl)</td>
<td>83.8 ± 2.6</td>
<td>85.6 ± 1.8</td>
<td>NS</td>
</tr>
<tr>
<td>Triacylglycerol (mg/dl)</td>
<td>127.7 ± 9.6</td>
<td>119.8 ± 7.0</td>
<td>NS</td>
</tr>
<tr>
<td>Total cholesterol (mg/dl)</td>
<td>232.8 ± 2.7</td>
<td>202.7 ± 6.7</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>HDL-cholesterol (mg/dl)</td>
<td>42.1 ± 2.6</td>
<td>41.7 ± 2.4</td>
<td>NS</td>
</tr>
<tr>
<td>LDL-cholesterol (mg/dl)</td>
<td>160.3 ± 2.8</td>
<td>133.2 ± 5.4</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>VLDL-cholesterol (mg/dl)</td>
<td>32.4 ± 4.2</td>
<td>27.1 ± 2.1</td>
<td>NS</td>
</tr>
<tr>
<td>Non HDL-c (mg/dl)</td>
<td>192.7 ± 5.7</td>
<td>160.3 ± 6.4</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>TC/HDL-c</td>
<td>6.0 ± 0.4</td>
<td>5.2 ± 0.4</td>
<td>NS</td>
</tr>
<tr>
<td>LDL/HDL-c</td>
<td>4.1 ± 0.3</td>
<td>3.4 ± 0.3</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>

The data are mean ± EE; n=38.

*Mean treatment difference (%) = [(after treatment x 100) / baseline] – 100, where baseline and after treatment represent the mean of the absolute values from weeks 1 and 8.

NS: no significant differences
Plasma lipids

**Total Cholesterol (TC), LDLc, Non-HDLc and TC-LDLc to HDLc ratios**

Significant changes were found in TC (p<0.001), LDLc (p<0.001), and Non-HDLc (p<0.001) for both, the -glucan and wheat whole group and AHA diet (Table 2). However, β-glucan supplementation achieved a stronger LDLc reduction from 167.9 ± 4.3 to 120.9 ± 4.3 mg/dl Vs. only 160.3 ± 2.8 to 133.2 ± 5.4 mg/dl obtained in group A. This represents a highly significantly 27.3% fall in LDLc concentration when comparing with a smaller 16.8% reduction in group A.

Non-HDLc exhibited a significantly drop in -glucan group from 191.5 ± 4.0 to 143.7 ± 3.7 mg/dl (-24.5%) compared with 192.7 ± 5.7 to 160.3 ± 6.4 mg/dl (-16.1%) reduction in group A, p<0.04.

The mean LDLc to HDLc ratio declined during wheat fiber from 4.1±0.3 to 3.4±0.3, p<0.03 and -glucan supplementation from 4.5±0.3 to 2.5±0.1, p<0.001). Comparing both schemes, this study showed a greater reduction in -glucan group (-42.1% vs.-13.3%, p<0.001) as well as TC to LDLc ratio (-33.3% Vs -8.4%; p<0.003).

No significant differences were observed for VLDLc and triglycerides within and between groups, when comparing baselines at week 8.

**HDLc behaviour**

During the study period, HDLc concentrations increased significantly only in -glucan intervention group from 39.4 ± 2.0 to 49.5 ± 2.1 mg/dl, p<0.00. Considering percentages, we found a strong 27.8% increase in HDLc concentration compared to a 2.2% decrease in whole wheat diet, p<0.001.

**Acceptability**

Data were made available for all participants explaining potential adverse effects of fiber (such as diarrhea, nausea, abdominal discomfort, abdominal distension, and flatulence). These factors were minimal for both diets, indicating slight awareness of symptoms that were easily tolerated.

All nutritional interventions were well accepted (Table 3). Each of the five attributes rated (appearance, color, aroma, flavor, and texture) had a median of 4 to 6 points in whole wheat bread and a median of 6 to 8 points in oat-derived -glucan, on a scale of 0 to 9 (Table 2). When comparing both breads, significant scores differences were found favoring to β-glucan bread in terms of appearance (p<0.001), flavor (p<0.003), and texture (p<0.001). No differences were found in aroma and color (Table 3).

**Discussion**

High plasma levels of low-density lipoprotein cholesterol, triglycerides and reduced levels of high-density lipoprotein cholesterol, is significantly associated with an increased incidence of CVD and the improvement of this states leads to a significant reduction of cardiovascular mortality.12,14 Thus, the combination of two lipidic risk factor calculated as index like LDL/HDL and TC/HDL ratios has also been used to estimate cardiovascular risk because improve sensitivity and specificity (6-8,20). Increasing evidence suggests that besides pharmacological treatment also lifestyle changes reduce the CVD risk.18,21 In this context, lifestyle factors such as physical activity and dietary behavior, particularly in subjects with an increased CVD risk, are in the center of interest19, whereas the positive physiological properties and metabolic benefits of complex carbohydrates such as fiber are still underestimated in prevention of atherosclerosis.15,18

Presently, the National Cholesterol Education Program/ American Heart Association (NCEP/AHA) Step I and Step II diets are recommended when attempting to lower cholesterol levels. These diets are low in saturated fat as well as total fat and are considered a high-carbohydrate diet. They have been shown to lower total and LDL cholesterol by 5-14%. However, an unfortunate side effect of a high carbohydrate diet is an increase in plasma triglycerides as a decrease in the beneficial HDL cholesterol, two factors that increase the risk of cardiovascular disease. An alternative diet in the treatment of hypercholesterolemia is one high in monounsaturated fatty acids (MUFAs). These diets replace the saturated fat typically consumed with foods high in MUFAs, resulting in a total fat consumption greater than that of the Step I and II diets. In contrast to the NCEP/AHA diets, diets high in MUFAs do not raise triglycerides or lower HDLs and may even promote a rise in HDL.

<table>
<thead>
<tr>
<th>Table 3. β-glucan and whole-wheat bread sensorial evaluation*</th>
<th>β-glucan bread</th>
<th>Whole-wheat bread</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>Appearance</td>
<td>8</td>
<td>5</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Color</td>
<td>6</td>
<td>6</td>
<td>NS</td>
</tr>
<tr>
<td>odor</td>
<td>8</td>
<td>6</td>
<td>NS</td>
</tr>
<tr>
<td>flavor</td>
<td>8</td>
<td>4</td>
<td>&lt;0.003</td>
</tr>
<tr>
<td>Texture</td>
<td>8</td>
<td>5</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Total</td>
<td>38</td>
<td>26</td>
<td>--</td>
</tr>
</tbody>
</table>

*Median score
cholesterol. The majority of research performed on MUFAs has utilized olive or canola oil, both excellent sources of MUFAs, as primary food sources. By investigating other sources of MUFAs, researchers may potentially discover additional foods that will have the same beneficial effect as olive and canola oils. An increase in food sources of MUFAs known to combat high cholesterol may promote increased adherence to a high-MUFA diet.

Integration of complex carbohydrates into the everyday food patterns by unprocessed food components such as oat products seems to be well feasible and has been shown to be a safe approach for cholesterol reduction without unpleasant side effects.32,35,37

The beneficial effect of oat products on the lipoprotein profile are ascribe to their soluble fiber compound, β-glucan.14,16 β-glucan from oats is nonstarch polysaccharide that is composed of β-(1→4)-linked glucose units, which are separated every 2-3 units by a single β-(1→3)-linked glucose unit.37,40

Most research studies using food as the soluble fiber source have fed oats or oat products. Brown et al. performed a meta-analysis of 67 controlled dietary studies and calculated that, for each gram of soluble fiber from oats, psyllium, or pectina, total cholesterol and LDL concentration decreased by ≈1.55 mg/dl (0.04 mmol/L). The meta-analysis showed no significant change in triacylglycerols and HDL. The observed changes appeared to be independent of study design treatment length, and dietary fat content. Others showed significantly lower total cholesterol and LDL concentrations were reported after the consumption of oat bran. Generally, no significant change was reported in triacylglycerol or HDL concentration when oatmeal or oat bran was included in the diet.14,34,37

The present studies showed that a mean daily 8-wk intake of 6 g β-glucan from oat bran administered in bread, had favorable effects on the serum lipoprotein profile. The oat-derived β-glucan use in this investigation (Nutrim-OB) lowered total cholesterol and raised HDLc concentrations significantly, since, group B elicited a significant increase (27.8%; p<0.001) on HDLc, when compared with AHA diet. This HDLc increase represents a break-down in therapeutic approach of this common dyslipidaemia because previous research with statins, fibrates or nicotinic acid has not evidenced higher elevations than oat β-glucan therapy. Although significant reductions in LDL concentrations were found in the present study (27.3% p<0.04).

A combination of factors and mechanisms appears to contribute to the reduction in lipids observed after the consumption of soluble fiber.14,34,37 Mechanisms suggested for the reduction in cholesterol after increased consumption of soluble fiber include increased excretion of bile acids or neutral sterols, increased catabolism of LDL cholesterol, and reduced absorption of fat 1-3. Increased viscosity of the gastrointestinal and intestinal contests can delay gastric emptying, decrease nutrient absorption, and interfere in micelle formation. Soluble fibers were shown to be fermented in the colon and thus to give rise to short-chain fatty acids that can be absorbed and may inhibit hepatic cholesterol synthesis. The viscosity in the intestine may depend, among other thing, on the solubility and molecular weight of β-glucan in their oat products, in turn, may lead to a low viscosity in the intestine.14,15,48

The mechanism for the increase in HDLc concentrations by oat β-glucan is unknown but some studies suggest that amount of β-glucan is the key determinant of HDLc concentration increases. Six grams of oat β-glucan were administered in this study that represents a higher amount than most of the studies in which oats were evaluated previously.1,34,47 Behall et al.35, however, argued that the solubility and viscosity of the β-glucan are more important than the amount consumed for the effect on serum lipids. An increase in HDLc levels was observed when oat gum was used (in contrast with oat bran) and the authors attributed this to the low solubility and the moderate molecular weight of the oat gum, which resulted in low viscosity in the gut.14,48 The oat β-glucan used in this study (Nutrim-OB) also had a low solubility and a low viscosity, and taking this data together we suggest that our finding may be due to a combination of higher β-glucan concentration plus the particular chemo-physical properties mentioned above.

The types of oats products used in different studies varied considerably. The β-glucan content of a good-quality commercial oat bran varies between 6% to 10%; wide ranges in concentration are found as result of different processing methods of the oat bran. The linear structure of β-glucan is very susceptible to depolymerization during processing of the oats. This lead to reduced viscosity and physiologic activity.

Non-HDLc is an important predictor of cardiovascular disease and represents cholesterol carried by all potentially pro-atherogenic apo B-containing particles, primarily VLDL, IDL, LDL lipoprotein (a) and chylomicron remnant. The Strong Heart Study, a population-based study of CHD, suggests that Non-HDL cholesterol index may be particularly useful in predicting CVD risk in patients with diabetes. According to our data -glucan elicited a significant decrease on Non-HDLc (24.5%) when compared with AHA diet alone (16.5%), p<0.04. These facts support oat-derived -glucan interaction with both, lipidic pro-atherogenic mechanism and the primary anti-atherogenic mechanism: the reverse cholesterol transport.

Oat β-glucan enriched-diet elicited a significantly reduction in body weight and body-mass-index when compared...
pared with AHA step II diet. Weight loss enhances insulin sensitivity and thereby glucose and lipoproteins profiles, of substantial improved as observed in TC-LDLc to HDLc ratios, and reflected in CHD risk reduction.

We also did not observed any significant effect of the background bread formulated with the addition of β-glucan consumption on gastrointestinal symptoms. Thus, when comparing both breads, significant scores differences were found favoring to -glucan bread (experimental group) in terms of appearance (p<0.001), flavor (p<0.003), and texture (p<0.001). The dose of 6g β-glucan was practical, as reflected in the volunteers’ high compliance.

In conclusion, the result of the present study suggest that 6g β-glucan from oat administered in bread and a high MUFAs diet, in addition AHA diet and exercise can reduce risk factors associated with CVD in overweight and mild hypercholesterolemic male subjects. These results changes in food ant nutrient intake without changing energy intake without changing energy intake.

References