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## Effects of Dietary Fiber Intake on Cardiovascular Risk Factors

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### 1. Introduction

A healthy dietary pattern is characterized by a high consumption of non-refined grains, legumes, nuts, fruits and vegetables; relatively high intake of total fat, mainly derived from olive oil; moderate to high intake of fish and poultry; dairy products (usually as yogurt or cheese) in small amounts; low consumption of red meat and meat products; and moderate alcohol intake, usually in the form of red wine with meals (Willett et al., 1995). Therefore, a high consumption of fiber-rich foods is one of the characteristic features of a healthy diet. Dietary fiber (DF) has received much attention in nutritional epidemiology. Observational studies have consistently shown that DF intake is associated with reduced cardiovascular risk, including ischemic heart disease (Rimm et al., 1996a; Todd et al., 1999; Liu et al., 2002; Mozaffarian et al., 2003a) and stroke (Ascherio et al., 1998; Oh et al., 2005; Salmeron et al., 1997)), and a lower risk of diabetes (Meyer et al., 2000; Liu, 2003b). Clinical trials have also suggested that DF supplementation has beneficial effects on risk factors, such as blood pressure, serum lipids, insulin sensitivity and diabetic metabolic control (Streppel et al., 2005b; Brown et al., 1999; Anderson et al., 2000; Chandalia et al., 2000a; Ludwig et al., 1999).

#### 1.1 Dietary fiber: Definition and classification

The role of DF in nutrition and health is well established (Anderson et al., 1990; Englyst, Wiggins, & Cummings, 1982). Knowledge of the beneficial effects of high DF diets toward the prevention of cardiovascular diseases and several types of cancer, as well as the inclusion of DF supplements in slimming diets, has led to the development of a large and

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yielding market for DF-rich products. Commonly consumed products include traditional foods (meat, dairy products, breakfast cereals, biscuits, breads, etc.) enriched with different amounts of fiber from various sources, as well as dietary supplements including tablets, capsules, etc.

Traditionally, DF referred to plant cell wall components that are not digestible by human or other mammalian gastrointestinal tract enzymes, but that may be degraded by anaerobic bacteria in the colon (Trowell, 1972). The recognition that polysaccharides added to foods, notably hydrocolloids, could have similar effects to those originating from plant cell walls led to a redefinition of dietary fiber to include "polysaccharides and lignin that are not digested in the human small intestine" (Trowell et al., 1976).

Non-starch polysaccharides (NSP) are the main constituents of DF and include a host of different polymers, highly variable in terms of molecular size and structure, as well as in monomeric composition. The main classes of non-starch polysaccharides are cellulose, hemicelluloses, pectins, and other hydrocolloids. However, some authors (Saura-Calixto F, 1988) have reported that a significant part of the starch content in foods, namely, resistant starch (RS) escapes digestion and absorption in the human small intestine, along with other dietary substances not included in the DF definition such as protein, oligosaccharides and certain polyphenolic compounds (Cummings & Macfarlane, 1991; Bravo, 1998; Saura-Calixto F, 1988; Asp et al., 1996; Prosky, 1999).

In general, the definition and delimitation of DF has been much debated and related both to physiological considerations and to methods that can be used for DF analysis in foods (Asp, van Amelsvoort, & Hautvast, 1996; Englyst, H.N. and Hudson, G.J., 1996; Englyst & Englyst, 2005; Englyst, Liu, & Englyst, 2007; IoM (Institute of Medicine), 2005; FAO/WHO (Food and Agriculture Organization/World Health Organization), 1998; EFSA (European Food Safety Authority), 2007).

Therefore, DF constitutes a heterogeneous group of compounds. The components included in DF can be classified according to their chemical properties, such as their ability to dissolve in water (soluble vs. insoluble fibers), their ability to be fermented by the colonic microflora (fermentable vs. non-fermentable fibers), or their viscosity (viscous vs. non-viscous fibers) (Slavin et al., 2009) (see Figure 1).

Thus, cellulose is insoluble in water, whereas pectins and hydrocolloids, such as guar gum and mucilages, may form highly viscous water solutions. RS is insoluble and indigestible due to its physical form or enclosure in cellular structures, whereas resistant oligosaccharides are readily soluble in water but do not form viscous solutions. The terms "soluble" and "insoluble" DF have been used in the literature to differentiate between viscous, soluble types of fiber (e.g. pectins) and insoluble components such as cellulose. The distinction was mainly based on their different physiological effects. However, this differentiation is method-dependent, and solubility does not always predict physiological effects.

According to this controversy, the U.S. Food and Nutrition Board (FNB) defines "total DF" as the sum of "DF", consisting of non-digestible carbohydrates and lignin that are intrinsic and intact in plants, and "functional fiber", consisting of isolated, non-digestible carbohydrate components with demonstrated beneficial physiological effects in humans (IoM (Institute of Medicine), 2005). The rationale behind this differentiation is that there is epidemiological

evidence for the beneficial effects of foods naturally high in DF, such as whole-grain cereals, some fruits and vegetables, and that DF can be regarded as a marker of such foods. The argument that the term “dietary fiber” should be restricted to non-starch polysaccharides of cell wall origin (Englyst, K.N. & Englyst, H.N., 2005; Englyst, K.N. Liu, & Englyst, H.N., 2007) has a similar rationale. Consequently, according to the FNB, documentation of the beneficial effects of added, functional fiber is required for inclusion in “total dietary fiber”.

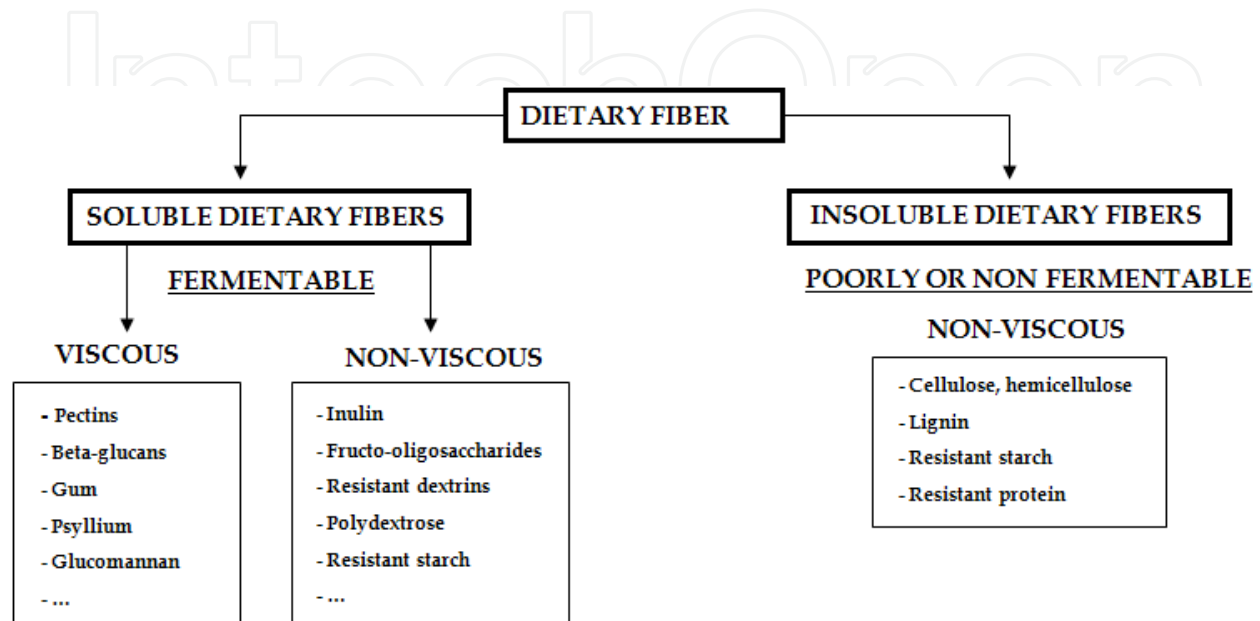


Fig. 1. Classification of dietary fiber according to chemical properties.

Based on this opinion, DF is defined as non-digestible carbohydrates plus lignin and it can be divided into different types:

- Non-starch polysaccharides (NSP) - cellulose, hemicelluloses, pectins, hydrocolloids (i.e. gums, mucilages, -glucans).
- Resistant oligosaccharides - fructo-oligosaccharides (FOS), galacto-oligosaccharides (GOS), other resistant oligosaccharides.
- Resistant starch - consisting of physically enclosed starch, some types of raw starch granules, retrograded amylose, chemically and/or physically modified starches.
- Lignin associated with the dietary fiber polysaccharides.

## 1.2 Methods for analysis of dietary fiber

Enzymatic-gravimetric or enzymatic-chemical methods for DF cover NSP, analytically resistant starch and lignin. However, as DF is a mixture of chemically heterogeneous carbohydrate components, several analytical methods are currently required to measure all fractions. Methods measuring only NSP (Englyst, H.N. & Hudson, G.J., 1996) give lower estimates than methods for total dietary fiber in foods containing resistant starch, and/or lignin. On the other hand, methods determining DF, including resistant starch, measure mainly retrograded amylose, resistant to the enzymes used in the assay. Finally, resistant oligosaccharides and inulin are not included in any of the current methods for total DF, and therefore need to be measured separately and subsequently added to the total fiber estimate (Cho et al., 1997; Champ et al., 2001, 2003)

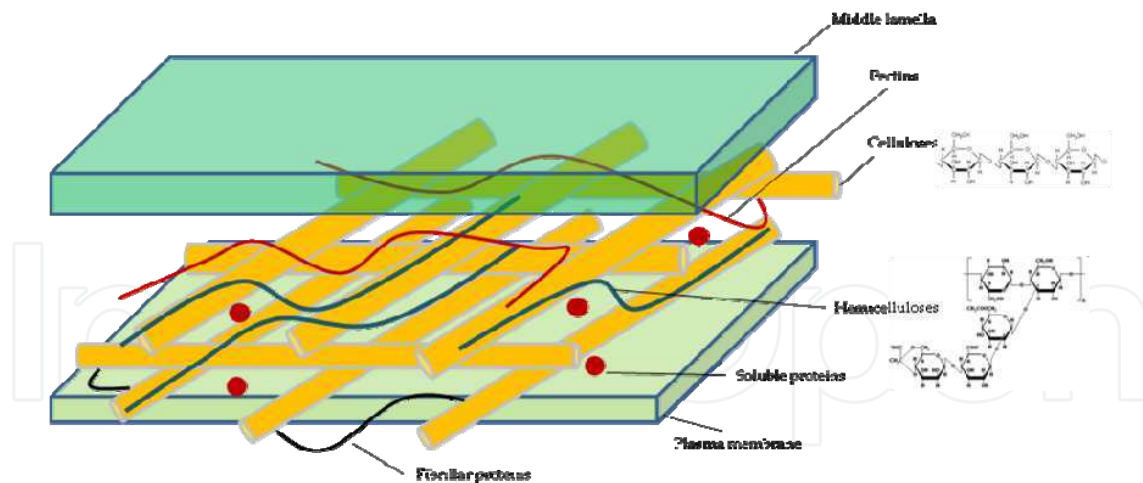


Fig. 2. The components that are part of the primary structure of the plant cell wall.

Total DF (TDF) can also be analysed by a combined enzymatic and gravimetric method, as the sum of insoluble DF (IDF) and soluble DF (SDF) which has been described in section 32.1.17 of the AOAC International Official Methods of Analysis (see Figure 3) based on previous work by Prosky et al. (Prosky et al., 1988). Another enzymatic-chemical method accepted for official action by the AOAC for the determination of TDF is one based on assays for components of TDF - neutral sugars, uronic acid residues and Klason lignin (section 45.4.11 AOAC). Starch is removed enzymatically and soluble polymers are precipitated with ethanol. Precipitated and insoluble polysaccharides are hydrolyzed using sulfuric acid and the released neutral sugars are quantitated as alditol acetates using gas-liquid chromatography. Uronic acids in the acid hydrolysate are determined by colorimetry. Klason lignin is determined gravimetrically.

However, other authors (Mañas & Saura-Calixto, 1995) have reported some methodological errors associated with precipitation and the enzymatic steps of the AOAC method. Subsequently, Saura-Calixto et al. (2000) proposed an alternative methodology to the AOAC definition of DF that measure the “indigestible fraction” (IF) of foods. The proposed method is an attempt to quantify, in a single analysis, the major non-digestible components in plant foods. This method is based on a concept of the IF that includes the main food constituents with nutritional relevance not available in the small intestine. In this method, samples are analyzed as eaten (fresh, boiled, or fried) and analytical conditions (pH, temperatures, incubation times) are close to physiological ones.

### 1.3 Dietary fiber content in foods

As we have mentioned before, DF occurring in foods and food products can be considered to consist mainly of cellulose, hemicelluloses, pectic substances, hydrocolloids (gums and mucilages), resistant starches, and resistant oligosaccharides.

SDF includes pectin, beta-glucans, inulin, fructans, oligosaccharides, some hemicelluloses, guar and gums. Food sources rich in SDF include legumes, vegetables, fruits, oat bran and psyllium seeds. IDF includes hemicellulose, cellulose, resistant starch and lignin. The main source of this kind of DF is whole grain. Vegetables and fruits contain both soluble and insoluble fiber, but depending on the vegetable and fruit type or maturity, the soluble to insoluble fiber ratio may vary.

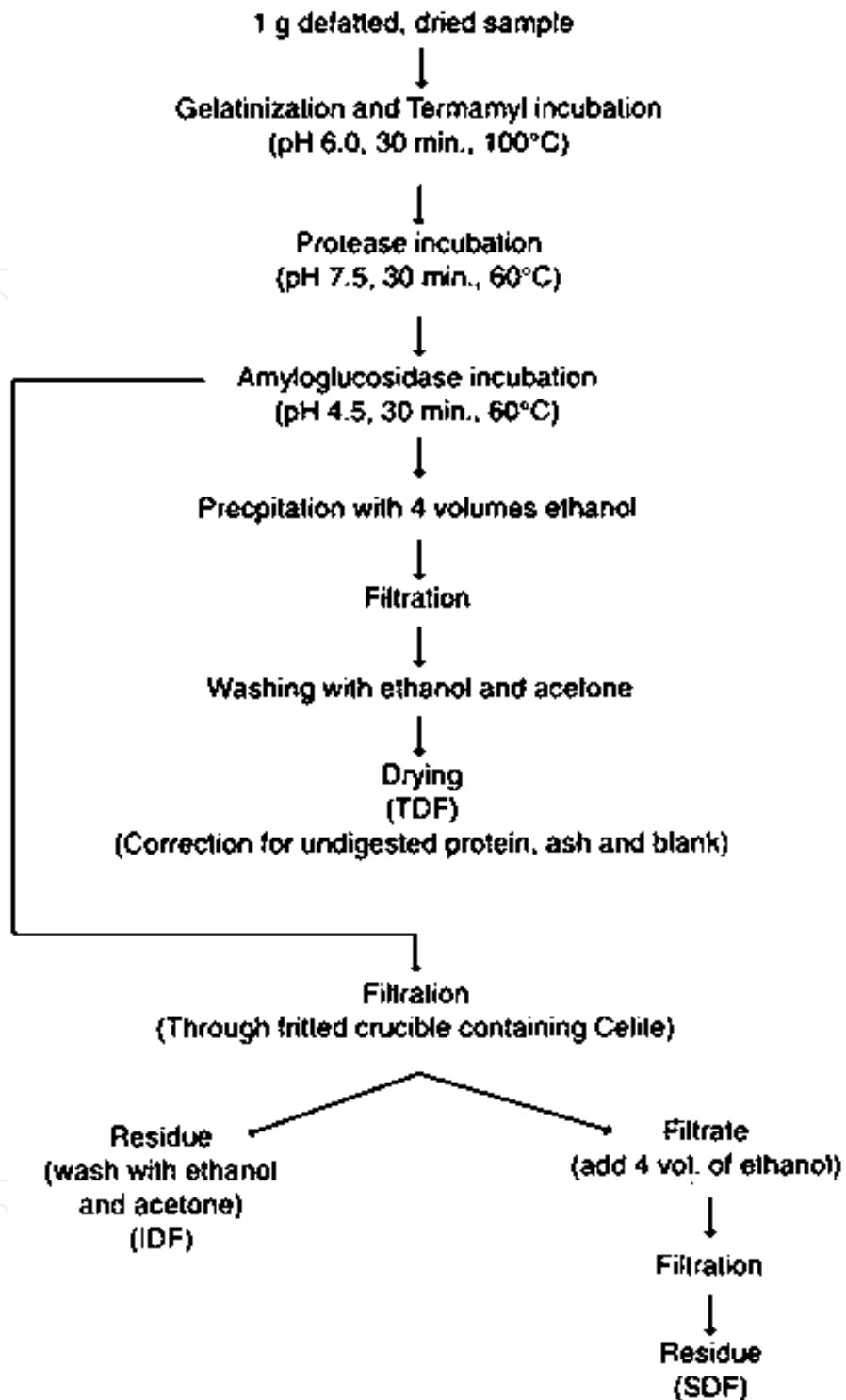


Fig. 3. Scheme of analysis of TDF by the AOAC method (section 32.1.17 of AOAC, 1995).

Table 1 includes data of soluble and IDF content in some DF rich foods analyzed according to AOAC methodology. The most complete database on DF content is the USDA National Nutrient Database for Standard Reference, Release 23 (USDA). Other institutions such as FAO have also published a database on food composition, INFOODS Food Composition Database for Biodiversity (FAO).

Fiber Food Source	Insoluble DF *	Soluble DF *	Total DF
<b>Vegetables, raw</b>			
Broccoli, raw	0.44	3.06	3.50
Cabbage, green, raw	0.46	1.79	2.24
Carrots, raw	0.49	2.39	2.88
Cauliflower, raw	0.47	2.15	2.62
Cucumber, raw, with peel	0.20	0.94	1.14
Lettuce, iceberg, raw	0.10	0.88	0.98
Onion, mature, raw	0.71	1.22	1.93
Pepper, sweet, green, raw	0.53	0.99	1.52
Tomatoes, red, ripe, raw	0.15	1.19	1.34
Spinach, raw	0.77	2.43	3.20
Beans, green, fresh, microwaved	1.38	2.93	4.31
Carrots, fresh, microwaved	1.58	2.29	3.87
Peas, green, froz., microwaved	0.94	2.61	3.54
Potato, white, boiled, w/o skin	0.99	1.06	2.05
<b>Fruits</b>			
Apple (Red delicious), raw, ripe w/skin	0.67	1.54	2.21
Avocado (California, Haas), raw, ripe	2.03	3.51	5.53
Bananas, raw, ripe	0.58	1.21	1.79
Grapefruit, raw, white, ripe	0.58	0.32	0.89
Grapes, raw, ripe	0.24	0.36	0.6
Mango, raw, ripe	0.69	1.08	1.76
Nectarine, raw, ripe, w/skin	0.98	1.06	2.04
Oranges (Navel), raw, ripe	1.37	0.99	2.35
Orange juice, retail, from concentrate	0.28	0.03	0.31
Peaches, raw, ripe, w/skin	1.31	1.54	2.85
Pears, raw, ripe, w/skin	0.92	2.25	3.16
Pineapple, raw, ripe	0.04	1.42	1.46
Plum, raw, ripe, w/skin	1.12	1.76	2.87
Prunes, pitted	4.50	3.63	8.13
Watermelon, raw, ripe	0.13	0.27	0.40
<b>Baked products</b>			
Bread, wheat	1.26	2.13	3.38

Fiber Food Source	Insoluble DF *	Soluble DF *	Total DF
Bread, whole-wheat	1.26	4.76	6.01
Bread, rye	1.62	2.84	4.46
Bread, reduced-calorie, white	1.01	8.46	9.47
<b>Cereal grains and pasta</b>			
White rice, long grain, cooked	0.00	0.34	0.34
Spaghetti, cooked	0.54	1.33	2.06
Cornflakes	4.28	0.5	3.78
Brown rice, long grain, cooked	0.44	2.89	3.33
Corn, sweet, white, cooked, boiled, drained, without salt	0.62	3.32	3.94
Oat bran, cooked	0.42	1.23	1.65
<b>Legumes</b>			
Chick peas, canned, drained	0.41	5.79	6.19
Cowpeas, canned, drained	0.43	4.11	4.53
Lentils, dry, cooked, drained	0.44	5.42	5.86
Pinto beans, canned, drained	0.99	5.66	6.65
Red kidney beans, can, drained	1.36	5.77	7.13
Split peas, dry, cooked, drained	0.09	10.56	10.65

Table 1. List of food with their insoluble, soluble, and total fiber content (g/100 g edible food portion as eaten). \* Data from Li et al., (Liu et al., 2002) and Marlett et al. (Marlett et al., 1992). Soluble and insoluble DF fractions were analyzed according to the AOAC Method 991.43.

#### 1.4 Dietary fiber intake

Typical intakes of carbohydrates and DF are presented for children and adolescents in 19 countries and for adults in 22 countries in Europe included in the EFSA Panel on Dietetic Products, Nutrition, and Allergies (EFSA Journal 2010). The data refer to individual based food consumption surveys conducted from 1994 onwards. Most studies comprise national representative population samples. The data were derived from national reports and from a published overview (Elmadfa, 2009).

The National Academies Press also published in their web ([www.nap.edu](http://www.nap.edu)) the book titled "Dietary Reference Intakes for Energy, Carbohydrate, Fiber, Fat, Fatty Acids, Cholesterol, Protein, and Amino Acids (Macronutrients)" in which Chapter 7 entitled "Dietary, Functional, and Total Fiber" summarizes the DF intake in the American population shown in the USDA database.

Table 2 shows the DF intake in the United States and European population adapted from the two most referenced databases (USDA and EFSA).



Life stage group	Total dietary fiber intake (USDA) g/day <sup>a</sup>	Total dietary fiber intake (EFSA) g/day <sup>b</sup>
<b>Infants</b>		
0–6 month	ND	ND
7–12 month	ND	ND
<b>Children</b>		
1–3 year	19	12–15
4–8 year	25	11–20
<b>Males</b>		
9–13 year	31	13–27
14–18 year	38	15–33
19–34 year	38	16–26
35–64 year	30	17–27
<b>Females</b>		
9–13 year	26	13–25
14–18 year	26	14–27
19–34 year	25	15–24
35–64 year	21	15–26

<sup>a</sup> Dietary reference intake values reported by the USDA (see [www.nap.edu](http://www.nap.edu))

<sup>b</sup> Dietary Reference intake values reported by the EFSA (EFSA Panel on Dietetic Products, Nutrition, and Allergies (NDA), 2010).

ND = Not determinable due to lack of data of adverse effects in this age group and concern with regard to the lack of ability to handle excess amounts.

Table 2. Dietary reference intakes of dietary fiber in United States and European population.

## 2. Main effects of dietary fiber

The physiological effects of DF result from its chemical and physical properties. Degradability, molecular weight, viscosity, particle size, cation exchange properties, organic acid absorption, and water-holding capacity are examples of such properties. Degradability enables the utilization of fiber in intestinal fermentation by colonic bacteria. Fermentation decreases the fecal pH and increases the bacterial biomass leading to an increase in faecal output and the production of gases and short-chain fatty acids (SCFAs). Viscous or soluble fibers form a gel by binding water and thereby decrease the gastric emptying rate and rate of absorption of glucose, triglycerides, and cholesterol. Large particle size and water holding capacity decrease transit time by increasing faecal bulk, which prevents constipation and dilutes carcinogenic compounds in the alimentary tract. Physicochemical properties are specific to different fibers and can change during cooking or digestion.

It is well known that DF plays important roles in the health of humans and in meeting the nutritional needs of animals. Much of the recent literature is focused on the ability of certain DF types to affect different physiological systems. Part of that research aims to understand how DF influences the characteristics and fermentation patterns of the intestinal microbiome

in humans (Meyer & Stasse-Wolthuis, 2009; Roberfroid et al., 2010). Consequently, it is possible to understand the prebiotic function of fibers using new DNA sequencing procedures that permit complete characterization of the bacterial populations (microbiome). One of the products of fermentation, butyrate, is able to regulate gene transcription which affects cell proliferation, differentiation, and apoptosis of colon cells (Wilson et al., 2010; Crim et al., 2008). The overall goals of these studies are to determine why some individuals are more at risk to develop diseases and some animals are more efficiently using their food for production purposes, as well as to identify dietary modifications that improve animal production efficiency and human health.

### **3. Mechanisms of the beneficial effects of dietary fiber**

Clinical recommendations for DF are routinely provided to improve gastrointestinal function, increasing laxation and reducing diverticular disease (Hall et al., 2010). In addition, an increase in the consumption of foods containing fiber is recommended to reduce obesity, type 2 diabetes mellitus (T2DM), cardiovascular disease and some cancers.

In this section we describe the mechanisms by which DF achieves its health effects focused on cardiovascular risk factors.

#### **3.1 Body weight**

DF can modulate body weight by various mechanisms, including promoting satiation, decreasing absorption of macronutrients, and altering the secretion of gut hormones.

Fiber rich foods usually have lower energy content, which contributes to a decrease into the energy density of the diet. Foods rich in fiber need to be chewed longer, leading to an increase in the time needed to eat the food and in the feeling of satiety. A number of studies (Slavin, 2005; Howarth et al., 2001a; Pereira & Ludwig, 2001) have shown that different DF affect subjective appetite, acute energy intake, long-term energy intake and body weight differently. The physicochemical properties of fibers may contribute to this variation. Fibers which make up viscous solutions and are more soluble and fermentable also delay the passage of food from the stomach to the duodenum and contribute to an increase in satiety and a decrease in energy intake. In the intestine, incorporation of fiber may complicate the interactions between digestive enzymes and their substrates, thereby slowing down the absorption of nutrients. It is also important to note that the effects of DF consumption on body weight may be related to different gut hormones which regulate satiety, energy intake and/or pancreatic functions (Aleixandre & Miguel, 2008).

#### **3.2 Hypocholesterolemic action**

The hypocholesterolemic action of fiber is partly mediated by a lower absorption of intestinal bile acid because of interruption of the enterohepatic bile acid circulation, thus increasing fecal bile acid loss, and its synthesis in liver (Morgan et al., 1993; Anderson et al., 1984). The physicochemical properties of soluble fiber result in important modifications in volume, bulk and viscosity in the intestinal lumen, which alter the metabolic pathways of hepatic cholesterol and lipoprotein metabolism, also resulting in the lowering of plasma LDL cholesterol. Other studies suggest that DF increases the enzymatic activity of cholesterol-7- $\alpha$ -

hydroxylase, the major regulatory enzyme in the hepatic conversion of cholesterol to bile acids (Roy et al., 2002) contributing to a higher depletion of hepatic cholesterol. Jones and co-workers (Jones et al., 1993) described a reduction in hepatic lipogenesis stimulated by insulin. It has also been suggested that the fermentation of DF by the intestinal microflora could modify the short chain fatty acid production thereby reducing acetate and increasing propionate synthesis. This, in turn, reduces the endogenous synthesis of cholesterol, fatty acids and very low density lipoproteins (Wolever et al., 1995; Wong et al., 2006).

Traditional dietary patterns, characterized by high fiber content, have been associated with lower rates of coronary disease. However, it should be taken into account that foods rich in fiber are also usually rich in a wide range of other bioactive substances which have a clear role in the prevention of cardiovascular disease (Craig, 1997; Hu & Willett, 2002; Buttriss & Benelam, 2010). Likewise, the beneficial effect of diets enriched in fiber on the lipid profile could also be explained by the fact that these diets are traditionally low in fat (especially saturated fat) and promote satiety and, therefore, help to protect against overweight and obesity (Mann, 2007).

### 3.3 Glucose tolerance and insulin sensitivity

Some studies have shown that soluble fiber plays an important role in controlling postprandial glycemic and insulin responses because of its effect on gastric emptying and macronutrient absorption from the gut (Slavin et al., 1999). Surprisingly, prospective studies have found that insoluble fiber, but not soluble fiber, is inversely related to the incidence of T2DM. In contrast, in postprandial studies, meals containing sufficient quantities of  $\beta$ -glucan, psyllium, or guar gum have decreased insulin and glucose responses in both healthy individuals and patients with T2DM. Diets enriched sufficiently in soluble fiber may also improve overall glycemic control in T2DM.

The association between the consumption of low dietary glycemic index (GI) foods and a lower risk of T2DM has been reported in several prospective studies (Salmeron et al., 1997), generally suggesting a preventive role of low GI diets. One of the largest was the 16-year follow-up of the Nurses' Health Study from 1980 including 3300 incident cases of type 2 diabetes, where the association between high glycemic load and the risk of developing T2DM was confirmed (Hu et al., 2001). A more recent meta-analysis of 37 prospective observational studies reported that diets with a high GI independently increased the risk of T2DM, providing protection similar to or higher than whole grains or fiber (Barclay et al., 2008). Similarly, a recent Cochrane database review concluded that low-GI diets can improve glycemic control in diabetic patients (Thomas & Elliott, 2009). However, not all investigators have reported similar findings: A well designed, controlled trial in well-controlled T2DM without oral antidiabetic therapy or insulin showed no effect on glycated hemoglobin, although a reduction in C-reactive protein and postprandial glucose was observed (Wolever et al., 2008).

To date, the physiopathologic mechanisms that explain the beneficial effects of fiber on glycemic control have still not been clearly delimited.

### 3.4 Blood pressure

Observational and experimental studies have reported that increased DF was associated with a lower risk of hypertension or lower self-reported blood pressure (BP), in both normotensive

and hypertensive subjects (Ascherio et al., 1992; Beilin, 1994; He & Whelton, 1999). Subjects consuming a vegetarian diet are generally at lower risk of developing hypertension. However, it is unknown whether this can be ascribed to the high fiber content of the diet because vegetarians—apart from differences in lifestyle—also have higher intakes of potassium, magnesium, and polyunsaturated fatty acids and a lower intake of saturated fat.

The differences observed in BP response might be explained by fiber dose, type of fiber consumed, or better compliance with dietary supplements than with high-fiber diets (He & Whelton, 1999).

### **3.5 C-reactive protein**

C-reactive protein (CRP) is a marker of acute inflammation recently recognized as an independent predictor of future cardiovascular disease and diabetes.

Several studies have reported that DF intake is inversely associated with serum concentrations of CRP (Butcher & Beckstrand, 2010; Oliveira et al., 2009). The mechanisms of change in CRP levels as a result of DF intake are still largely unknown; possibilities include DF slowing the absorption of glucose, fiber-rich meal modulation of cytokine responses blunting oxidative stress and inflammation, and the production of anti-inflammatory cytokines by gut flora exposed to fiber.

## **4. Epidemiological studies**

Several limitations are common to all prospective studies examining the relationship between foods and nutrients and disease risk. The lack of consistency in the methods used for the measurement of different classes and subgroups of dietary fiber, especially the NSP, complicates comparisons between the results of studies and their extrapolation into nutritional recommendations. However, prospective epidemiological studies provide strong evidence for a protective role of wholegrain cereals, fruits and vegetables and dietary patterns characterized by relatively high intakes of such foods.

While a high consumption of DF derived from cereals is also associated with a reduced risk of cardiovascular disease, it is not clear whether this cardioprotection can entirely be attributed to the polysaccharides per se. Even the best prospective studies cannot conclusively eliminate the possibility of residual confounding, thus recommendations regarding the intake of carbohydrates in relation to cardiovascular disease also depend on the intervention studies described below.

### **4.1 Body weight**

Large prospective studies have reported that consumption of DF is inversely associated with weight and weight gain. A high intake of DF may assist weight loss because of the incomplete digestion and absorption of energy from this type of carbohydrates and the bulky nature of high-fiber foods, with increased demands on chewing and subsequent distension and delayed emptying of the stomach, promoting satiety and thereby curtailing energy intake.

Reviews of randomized trials in adults have shown weight loss in a majority of studies with no differences between fiber types or between fiber occurring in foods or in supplements

(Pereira & Ludwig, 2001; Howarth et al., 2001a). Results from seven prospective cohort studies show an inverse relationship between weight gain and baseline intake or change in fiber intake among adults during follow-up periods of up to 12 years (Lairon, 2007; Koh-Banerjee et al., 2004).

The CARDIA (The Coronary Artery Risk Development in Young Adults) study, a multicenter population-based cohort study carried out over 10 years, examined 2909 young individuals to determine the relationship between total dietary fiber intake and plasma insulin concentrations, weight and other cardiovascular disease risk factors. After adjusting for BMI and multiple dietary and potential non-dietary confounders, the study reported an inverse association between total fiber intake, plasma insulin concentrations and body weight gain (Ludwig et al., 1999) suggesting that fiber may play an important role in the prevention of insulin resistance and obesity. Individuals consuming higher amounts of fiber had a lower weight gain compared to those consuming lower amounts, independently of the level of total fat consumed. Similarly, in the Nurses' Health Study cohort Liu (2003) showed that women in the highest quintile of DF intake had a 49% lower risk of major weight gain than women in the lowest quintile.

Kromhout et al. (2001) investigated the association between DF and indicators of body fat in a cross-cultural study of 16 cohorts of 12 763 middle-aged men in seven countries, between 1958 and 1964. The average DF intake was inversely related to population average subscapular skinfold thickness and body mass index.

Alfieri et al. (1995) assessed the total fiber intake by means of 3-day food records in 3 population groups (one normal, one moderately and one severely obese group). These authors showed that fiber intake was significantly higher in the normal weight group and was inversely associated with BMI after adjusting for several potential confounders. Recently, new research conducted as part of the PREDIMED study has also shown a significant inverse relationship between TDF consumption and body mass index or abdominal circumference (Estruch et al., 2009).

In an observational study looking at the effect of overall diet on body composition in obese and lean subjects it was demonstrated that lean men and women had significantly higher fiber intake versus obese males and females (27.0 g/d and 22.7 g/d vs. 22.0 g/d and 15.0 g/d respectively) (Miller et al., 1994). These results were supported in another study with a cohort of over 5000 subjects, which showed that higher fiber intake is associated with a lower body mass index (BMI) in both men and women (Appleby et al., 1998).

In a prospective cohort with 252 premenopausal, non-smoker women free from serious disease, Tucker & Thomas (2009) conducted a study to determine whether changes in fiber intake (total, soluble, and insoluble) influence the risk of gaining weight and body fat over time (20 months). Increasing DF significantly reduces the risk of women gaining weight and fat. For each 1 g increase in total fiber consumed, weight decreased by 0.25 kg ( $P = 0.0061$ ) and fat decreased by 0.25 percentage point ( $P = 0.0052$ ). Controlling for potential confounders did not affect the relationships, except for changes in energy intake, which weakened the associations by 24-32%. Soluble and insoluble fibers were borderline predictors of changes in weight and fat.

Studies on children eating mixed diets do not indicate adverse effects on growth due to high fiber intake. On the other hand, there are studies indicating that DF intake can contribute to lowering the risk of obesity in this population group (Edwards & Parrett, 2003).

In conclusion, increased intake of DF, both from naturally fiber-rich foods and added fiber or fiber supplements, has been shown to be related to improved weight maintenance in adults and sustained weight reduction in overweight subjects. Estimated intakes associated with this effect in adults are in the order of >25 g DF per day (from wholegrain cereals, fruit and vegetables).

#### 4.2 Hypocholesterolemic action

DF has a potentially important effect on lipids and lipoproteins when consumed in plant foods or as supplements. Viscous subgroups of DF, including pectins,  $\beta$ -glucans, glucomannans, guar and psyllium, which are generally water soluble, all lower total and LDL cholesterol between 5 and 10 g/day, lowering LDL by about 5% (Truswell, 2002).

A cross-sectional epidemiological data, based on the EURODIAB Complications Study, which included over 2000 patients in 31 European centers, showed an inverse association between DF intake and HbA<sub>1c</sub> and LDL cholesterol (in men only) and a positive association with HDL cholesterol in men and women (Toeller et al., 1999).

In an analysis of dietary factors and cardiovascular risk performed in a sample of 3,452 Swiss adults, it was observed that a healthy diet characterized by high consumption of DF was associated with lower rates of serum triglycerides and higher HDL-c (Berg et al., 2008). A 10-year study of a cohort of 2,909 healthy adults aged between 18 and 30 showed a strong negative association between fiber intake and blood pressure and levels of triglyceride, HDL cholesterol, LDL cholesterol, and fibrinogen even after adjusting for confounding factors (Ludwig et al., 1999). In a cohort of 316 Japanese-Brazilian subjects, a decrease of 12.5 mg/dl was observed in the serum total cholesterol levels ( $P < 0.05$ ) for each increase of 10 g in the consumption of DF intake in a 7-year follow up (de Castro et al., 2006). Wu et al. (2003) studied a cohort of 573 adults aged between 40 and 60 and found an inverse relationship between the ratio of TC/HDL-c and the total intake of DF ( $P = 0.01$ ); the ratio of TC/HDL-c has been proposed as a good indicator of cardiovascular risk.

Van Dam RM, et al. (2003) performed a cross-sectional study of 19,750 randomly selected men and women aged 20-65 y from 3 Dutch municipalities. Three dietary factors were identified: Cosmopolitan pattern (rich in fried vegetables, salad); traditional pattern (rich red meat) and refined pattern (rich sugar-beverages and white bread). A higher adherence to the Cosmopolitan pattern was significantly associated with lower blood pressure and higher HDL-c concentrations; the traditional dietary pattern was associated with higher blood pressure and higher concentrations of HDL cholesterol, total cholesterol, and glucose; and the refined dietary pattern was associated with higher total cholesterol concentrations.

Whole grain was also inversely associated with total cholesterol ( $P$  for trend = 0.02), LDL cholesterol ( $P$  for trend = 0.04), and 2-h glucose ( $P$  for trend = 0.0006) in a cross-sectional analysis of 1516 community-dwelling participants in the Baltimore Longitudinal Study of Aging. Associations between cereal fiber and anthropometrics and plasma lipids were similar (Newby et al., 2007).

In conclusion, viscous types of DF mainly from fruits, vegetables and whole grains may contribute to reducing total and LDL-cholesterol concentrations. The effects are limited to amounts usually consumed from foods.

### 4.3 Glycemic index and Type 2 diabetes mellitus

Glycemic control is of crucial importance in the management of T2DM. Few intervention studies have investigated the effects of fiber intake on measures of glucose tolerance or insulin sensitivity, but recent observations have shown the favourable effects of a diet with abundant fiber-rich foods, particularly whole grain, bran and germ intake, on the risk of T2DM (Murakami et al., 2005; Krishnan et al., 2007; Schulze et al., 2007; de Munter et al., 2007).

In the Nurses' Health Study, wholegrain consumption appeared to be protective for T2DM. When comparing the highest and lowest quintiles of intake, the age and energy adjusted relative risk was 0.62 (95% CI: 0.53, 0.71). Further adjustment for other risk factors did not appreciably alter this risk estimate (Liu et al., 2000; Salmeron, et al., 1997) virtually identical risk reduction was observed among men participating in the Health Professionals Study (Fung et al., 2002). A relative risk of 0.63 was reported in association with three or more servings/day of wholegrain. In the Iowa Women's Health Study, postmenopausal women in the upper quintile of wholegrain consumption (more than 33 servings per week) were 20% less likely to develop T2DM than those in the lowest quintile (fewer than 13 servings per week) (Meyer et al., 2000). Cereal fiber appears to be associated with a protective dose-response effect that is present after controlling for a range of potentially confounding factors. The role of whole grains and DF in diabetes has been reviewed in detail by Venn and Mann (Venn & Mann, 2004).

Two large cross-sectional studies, using validated food frequency questionnaires to assess nutrient intake and either the frequently sampled intravenous glucose tolerance test or homeostasis model assessment for insulin resistance, found that intake of DF was inversely associated with the probability of having insulin resistance (Lau et al., 2005; Liese et al., 2005) and it was possible to demonstrate that fiber was associated with increased insulin sensitivity even after adjustment for body mass index.

During 8 years of follow-up (1995-2003) 1964 incident cases of T2DM were reported in a prospective cohort study including 41,186 participants of the Black Women's Health Study without a history of diabetes or CVD. Daily consumption of whole grain was associated with a lower risk of T2DM compared with consumption less than once a week. After mutual adjustment, the hazard ratio was 0.73 (0.63-0.85;  $P$  for trend = 0.0001) for whole grains (van Dam et al., 2006).

Krishnan S et al. (2007) examined the association of glycemic load, GI, and cereal fiber with risk of T2DM in 59000 black women with T2DM, CVD or cancer from the Black Women's Health Study. During 8 years of follow-up, there were 1,938 incident cases of diabetes. GI was positively associated with the risk of diabetes: the incidence rate ratios (IRR) for the highest quintile relative to the lowest was 1.23 (95% CI, 1.05-1.44). Cereal fiber intake was inversely associated with the risk of T2DM with an IRR of 0.82 (95% CI, 0.70-0.96) for the highest *vs.* the lowest quintiles of intake. Stronger associations were seen among women with a body mass index lower than 25: IRRs for the highest *vs.* the lowest quintile were 1.91

(95% CI, 1.16-3.16) for GI ( $P = 0.12$ ) and 0.41 (95% CI, 0.24-0.72) for cereal fiber intake ( $P = 0.05$ ).

In conclusion, increasing intakes of foods rich in DF are associated with a reduced risk of developing T2DM. DF intakes associated with favorable effects are about 25 to 30 g per day, although the contribution of DF per se to this effect remains to be established.

#### 4.4 Blood pressure

Increased DF has been associated with a lower risk of hypertension, and a meta-analysis of clinical studies of fiber supplementation also supports an inverse association between fiber and blood pressure.

In a cross-sectional study, Lairon D et al. (2007) determined the quintiles of fiber intake from dietary record, separately for 2532 men and 3429 women. The highest total DF and insoluble DF intakes were associated with a significantly ( $P < 0.05$ ) lower risk of overweight and elevated waist-to-hip ratio, BP, plasma apolipoprotein (apo) B, apo B:apo A-I, cholesterol, triacylglycerols, and homocysteine. Fiber from cereals was associated with a lower body mass index, BP, and homocysteine concentration; fiber from vegetables with a lower BP and homocysteine concentration; and fiber from fruit with a lower waist-to-hip ratio and BP. Fiber from dried fruit or nuts and seeds was associated with a lower body mass index, waist-to-hip ratio, and fasting apo B and glucose concentrations.

Estruch et al. (2009) analyzed 772 cardiovascular high-risk subjects (age  $69 \pm 5$  years). On randomization they were assigned to a low-fat diet or two recommendations for increasing vegetable, fruit and legume intake. Body weight, waist circumference and mean systolic and diastolic BP significantly decreased across the quintiles of fiber intake ( $P < 0.005$ ).

In a meta-analysis of randomized placebo-controlled trials to estimate the effect of fiber supplementation on BP overall and in population subgroups, fiber supplementation (average dose, 11.5 g/d) changed systolic BP by  $-1.13$  mm Hg (95% CI:  $-2.49$  to  $0.23$ ) and diastolic BP by  $-1.26$  mm Hg ( $-2.04$  to  $-0.48$ ). Reductions in BP tended to be greater in older ( $>40$  years) and in hypertensive populations than in younger and in normotensive subjects (Streppel et al., 2005).

#### 4.5 Cardiovascular disease

Many epidemiological studies have evaluated the effects of DF on the risk of coronary heart disease (CHD) (Rimm et al., 1996; Todd et al., 1999; Liu et al., 2002; Mozaffarian et al., 2003). Most likely, as assessed in prospective studies, DF intake with the usual diet is a marker of healthy food choices with an overall cardiovascular benefit, while changing the diet to increase DF at late stages, when clinical consequences of atherosclerosis have developed, may not be protective.

A meta-analysis, involving four of the largest studies published, suggested a 28% reduction in the risk of CHD on comparing individuals in the highest and lowest quintiles of intake of whole grains (relative risk 0.72, 95% confidence intervals: 0.48, 0.94) (Anderson, 2003).

After adjustment for cardiovascular risk factors, in the Iowa Women's Health Study the relative risks for cardiovascular disease were 1.0, 0.96, 0.71, 0.64 and 0.70 in ascending



quintiles of whole grain intake,  $P < 0.02$  (Jacobs et al., 1998). The Nurses' Health Study (Liu et al., 2000) observed risk reductions of magnitude similar to those observed for CHD (relative risk 0.69, 95% CI: 0.50, 0.98 when comparing the highest relative to the lowest quintile of intake of whole grains).

The suggestion that reduced cardiovascular risk principally results from consumption of wholegrain rather than DF was supported by findings from the Iowa Women's Health Study. CHD rates were compared in women consuming similar amounts of cereal fiber from either predominantly refined grain sources or predominantly wholegrains. After adjustments, all-cause mortality was significantly lower, and CHD appreciably (though not statistically significantly) reduced among the latter group (Jacobs et al., 2000).

In the Nurses' Health Study and the Health Professionals' Study (Hu et al., 2000; Fung et al., 2001), factor analysis was used to examine the association between CHD and the two major dietary patterns identified: "western" characterized by higher intakes of red and processed meats, sweets and desserts, French fries and refined grains and 'prudent' characterized by higher intakes of fruit, vegetables, legumes, fish, poultry and wholegrains. After adjustment for cardiovascular risk factors, the prudent diet score was associated with relative risks of 1.0, 0.87, 0.79, 0.75 and 0.70 from the lowest to the highest quintiles. Conversely, the relative risks across increasing quintiles of the western pattern score were 1.0, 1.21, 1.35, 1.40 and 1.64. The patterns were also related to biochemical markers of CHD.

The effect of DF may be largely explained by fiber derived from wholewheat, rye or pumpernickel breads, in a multicenter study among 3588 men and women aged 65 years or older and free of known CVD at baseline (Mozaffarian et al., 2003). During a mean follow-up of 8.6 years, there were 811 incident CVD events. After adjustment for different confounder factors, cereal fiber consumption was inversely associated with incident CVD ( $P$  for trend=0.02), with 21% lower risk (HR: 0.79; 95% CI: 0.62-0.99) in the highest quintile of intake, compared with the lowest quintile. In similar analyses, neither fruit fiber intake ( $P$  for trend=0.98) nor vegetable fiber intake ( $P$  for trend=0.95) were associated with incident CVD.

Furthermore, in a combined analysis of 10 prospective cohort studies conducted in the USA and Europe Pereira et al. (2004) showed a 25% decrease in the risk of CHD for each 10 g increase in fiber intake, after adjusting for several dietary and cardiovascular confounding factors. A relative risk of 0.90 (95% CI: 0.77, 1.07 that is not statistically significant) was reported for total CHD events for each 10 g/day increase in cereal fiber. When considering CHD deaths, the relative risk, 0.75 (95% CI: 0.63, 0.91) was statistically significant, the association being independent of a number of dietary factors and other cardiovascular risk factors.

Recently, Streppel et al. (2008) also observed that CHD mortality and all-cause mortality were reduced by 17% and 9%, respectively for every additional 10 g of DF per day, with no clear associations for different types of DF.

#### 4.6 Inflammatory markers

CRP is an inflammatory marker useful in the prediction of coronary events. Results from recent epidemiologic studies have consistently shown an inverse association between DF intake and plasma CRP levels. In a recent study, both increasing fiber intake by about 30 g/day from a diet rich in fiber or from a supplement reduced the levels of CRP.

Jenkins et al. (2003) reported reduced CRP levels in hyperlipidaemic patients consuming a high carbohydrate diet rich in viscous fiber-containing foods. However, the diets were also high in nuts (almonds), plant sterols and soy proteins, and it is therefore impossible to disentangle separate effects. A recent study (Kasim-Karakas et al., 2006) found that when carbohydrate replaced a substantial proportion of dietary fat under eucaloric conditions, the levels of several inflammatory markers increased along with an increase in triglycerides.

Data from the Massachusetts Hispanic Elders Study (Gao et al., 2004) obtained from 445 Hispanic and 154 non-Hispanic white elders showed that greater frequency of fruit and vegetable intake, which are rich in fiber, was associated with lower CRP and homocysteine concentrations. With each additional serving of fruit and vegetable intake, the risk of having high CRP (>10 mg/l) and homocysteine concentrations decreased by 21% and 17%, respectively.

The relation between DF and CRP was examined from 1999 to 2000 in 3,920 participants in the National Health and Nutrition Examination Survey (Ajani, Ford, & Mokdad, 2004). DF intake was inversely associated with serum CRP concentrations: The adjusted odds ratio for increased CRP levels (>3 mg/l) was 0.59 ( $P = 0.006$ ) for the highest quintile of fiber intake compared with the lowest. The results were not affected after exclusion of persons with diabetes, cancer, CVD, or CRP levels >10 mg/l. The results of Ajani et al. confirmed the previous findings (King et al., 2003).

## 5. Clinical trials

Most of the data available on disease prevalence and events are from epidemiological studies. However, it is necessary to also resort to clinical trials to test effects of different types and sources of DF on cardiovascular risk factors taking into account a specific population.

### 5.1 Body weight

Although epidemiological data and mechanistic studies support the contention that fiber has beneficial effects on body weight regulation; there has been inconsistent data from randomized controlled clinical trials that have evaluated how body weight is affected by supplementing fiber in the diet (Rodriguez-Moran et al., 1998; Birketvedt et al., 2000; Pittler & Ernst, 2001).

In a systematic review, Howarth et al. (2001) analyzed several clinical trials conducted in small and heterogeneous population samples over relatively short periods of time (from 1 to 12 months). The findings were that the intake of 12 g fiber/day resulted in a decrease of 10% in energy intake and a body weight loss of 1.9 kg over 3.8 months, with this effect on body weight loss being greater in obese subjects.

Esposito et al. (2004) explored the possible mechanisms underlying a dietary intervention and randomized 180 patients (99 men, 81 women) with the metabolic syndrome to a Mediterranean-style diet (instructions about increasing daily consumption of whole grains, vegetables, fruits, nuts, and olive oil) versus a cardiac prudent diet with fat intake less than 30%. After 2 years, body weight decreased more in the intervention group than in the control group, even after controlling for weight loss, inflammatory markers, such as IL-6, IL-7, IL-18, and CRP.

In randomized placebo-controlled studies, 176 overweight or obese men and women were included to receive either active fiber substance or placebo during a five-week observation period. The fiber supplements consisted of the viscous fibers glucomannan (Chrombalance), glucomannan and guar gum (Appe-Trim) and glucomannan, guar gum and alginat (Glucosahl). All fiber supplements plus a balanced 1200 kcal diet induced a significant weight reduction more than placebo and diet alone, during the observation period (Birketvedt et al., 2005).

Salas-Salvador et al. (2008) evaluated the effect of a mixed fiber supplement on body-weight loss, in 200 overweight or obese patients in a parallel, double-blind, placebo-controlled clinical trial. Weight loss tended to be higher after both doses of fiber ( $-4.52 \pm 0.56$  and  $-4.60 \pm 0.55$  kg) than placebo ( $-0.79 \pm 0.58$  kg); the differences in changes between groups were not statistically significant. Postprandial satiety increased in both fiber groups compared to the placebo. Estruch et al. (2009) analyzed 772 cardiovascular high-risk subjects that were assigned to a low-fat diet or two recommendations for increasing the intake of vegetables, fruit and legumes. Body weight, waist circumference and BP significantly decreased across the quintiles of fiber intake ( $P=0.04$ ).

In a dietary intervention involving 107 overweight and obese children it was shown that low GI diets are more effective in reducing weight than low-fat diets (Spieth et al., 2000). The BMI of subjects assigned to the low GI diet reduced significantly in comparison to those on the low-fat diet across all three tertiles ( $<28.3$  kg/m<sup>2</sup>,  $28.3$ – $34.9$  kg/m<sup>2</sup> and  $>34.9$  kg/m<sup>2</sup>). The mean overall reduction was  $1.53$  kg/m<sup>2</sup> vs.  $0.06$  kg/m<sup>2</sup> ( $P < 0.001$ ). Another study showed that low GI diets result in the greatest reduction in fat mass, especially in women (McMillan-Price et al., 2006).

## 5.2 Serum lipids

Several studies have shown that a high consumption of DF, particularly soluble fiber (pectin, guar gum,  $\beta$ -glucans, glucomannan, and psyllium), significantly decreases serum levels of total and LDL cholesterol (Anderson, 2000; Brighenti, 2007). Other clinical trials support the hypocholesterolemic effects of soluble fiber derived both from supplements or fiber derived from foods in patients at high risk of cardiovascular disease.

In a double-blind placebo-controlled study, Rodríguez-Morán M et al., (1998) determined the plasma-lowering effects of *Plantago psyllium*, as an adjunct to dietary therapy, on lipid and glucose levels, in patients with T2DM. The study included 125 subjects undergoing a 6-week period of diet counseling followed by a 6-week treatment period in which *Plantago psyllium* or placebo was given in combination with a low fat diet. No significant changes were observed in the patient's in either group. Fasting plasma glucose, total cholesterol, LDL-c, and triglyceride levels, showed a significant reduction ( $P < 0.05$ ), whereas HDL-c increased significantly ( $P < 0.01$ ) following *Psyllium* treatment.

A meta-analysis carried out by Brown et al. (1999) indicates that the effects of different types of viscous fibers on TC concentrations are modest. These results were obtained from 67 experimental metabolic studies carried out on 2,990 subjects showing that for each gram of soluble fiber added to the diet, the TC and the LDL-c concentration decreased by  $1.7$  mg/dL and  $2.2$  mg/dL, respectively.

In a meta-analysis of 8 controlled trials, it was observed that the hypolipidemic effects of psyllium in hypocholesterolemic individuals already consuming a low-fat diet achieved reductions with diet only. Results confirm that *Psyllium* significantly lowers an additional 4% of serum total and cholesterol and an additional 7% relative of LDL-c concentrations in comparison to a placebo group consuming a low fat diet (Anderson, 2000).

In a randomized, crossover study Maki KC et al. (2007) compared the effects of consuming high-fiber oat and wheat cereals on postprandial metabolic profiles in healthy men. Twenty-seven subjects received oat (providing 5.7 g/day beta-glucan) or wheat (control) cereal products, in random order, incorporated into their usual diets for two weeks. Peak triglyceride concentration was lower after oat vs. wheat cereal consumption. Mean area under the triglyceride curve also tended to be lower.

In a recent parallel, double-blind, placebo-controlled clinical trial, 200 overweight or obese patients were randomized to receive a mixed dose of soluble fiber (3 g *Plantago ovata* husk and 1 g glucomannan) or a placebo twice or three times daily in the context of an energy-restricted diet for a period of 16 weeks. Differences in plasma LDL-c changes between the groups were significant, with greater reductions in the two fiber supplemented groups in comparison to the placebo (Salas-Salvado et al., 2008).

Insoluble fiber, such as that from wheat or cellulose, has not been reported to have any significant effect on blood cholesterol (Jenkins et al., 2000; Sola et al., 2007), possibly because of the presence, along with DF, of several bioactive and antioxidant phytochemical substances in foodstuffs (Salas-Salvado et al., 2006) or because of the effect that fiber has on blood pressure, body weight and postprandial glycemia or insulin levels.

### 5.3 Glycemic index and type 2 diabetes mellitus

On glycemic control, several randomized controlled trials have been performed to determine the effect of DF on insulin sensitivity, blood glucose control and hypoglycemic episodes. However, all were short-term studies. A whole grain diet led to a postprandial improvement in insulin sensitivity when compared to a refined grain diet. Plasma glucose concentrations were significantly lower for the high fiber diet than for the low-fiber diet. In clinical studies using fiber supplements, it appears that only soluble fiber plays a significant role in reducing postprandial glycemia. However, prospective epidemiological studies have shown that insoluble fiber, but not soluble fiber, from natural food sources was inversely related to the risk of diabetes.

Giacco and co-workers (Giacco et al., 2000) carried out a 6-month randomized parallel study comparing a diet containing 50 g/d of soluble fiber with a diet containing only 15 g/d of fiber. Thirty-two patients (intervention group) and 31 patients (control group) were randomized to follow a high-fiber or low-fiber diet for a 24-week period. This study confirmed the potential for around 40 g/d DF (half of the soluble type from legumes, fruits and vegetables) to improve glycemic control. They found an improvement in the daily blood glucose profile and the HbA<sub>1c</sub> levels, as well as a marked reduction in the number of hypoglycemic events.

Chandalia et al. (2000) also demonstrated that high-fiber diets contributed to better metabolic control in 13 T2DM diabetic patients. In a cross-over study, patients were

randomized to a diet containing a moderate amount of fiber (8 g of soluble fiber and 16 g insoluble fiber) or to a diet containing a high amount of fiber (25 g of soluble fiber and 25 g insoluble fiber). Plasma glucose concentrations were significantly lower for the high fiber than for the low-fiber diet.

In a controlled 6-week study, overweight hyperinsulinaemic adults consumed diets providing 55% energy from carbohydrate and 30% from fat, Pereira et al. (Pereira et al., 2002) observed that insulin sensitivity measured by a euglycemic hyperinsulinaemic clamp was appreciably improved in the wholegrain compared with the refined grain diet. Fasting insulins and area under the 2-h insulin curve were lower, despite body weight not being significantly different in the two diets. In this intervention, carbohydrates were derived from predominantly wholegrain or refined grain cereals, with DF content of the wholegrain diet 28 g compared with 17 g on the refined grain diet. DF was predominantly from cereal sources. Total carbohydrate and fat and fat sources were virtually identical in the two diets. Rye bread has also been shown to improve insulin sensitivity in overweight and obese women too (Juntunen et al., 2003).

Likewise, Weicker and co-workers (Weickert et al., 2006) used the same method to measure insulin sensitivity in overweight and obese women and found that this increased after 3 days of a diet containing bread enriched with insoluble fiber compared to another diet containing white bread

In a recent 6-month parallel, randomized clinical trial composed of 210 patients with T2DM the patients were randomized to either a high cereal fiber diet (GI = 80.8) or a low GI diet (GI = 69.6). The low GI diet resulted in statistically significant reductions in fasting plasma glucose and HbA<sub>1c</sub> (Jenkins et al., 2008). The results of this study confirm the notion that high fiber diets in a low GI setting are more effective in managing and preventing T2DM in comparison with high fiber diets that have medium or high GI.

A recent meta-analysis of randomized controlled trials looking at the effect of legumes on glycemic markers concluded that legumes as part of a high fiber diet significantly reduce fasting blood glucose and glycated proteins (Sievenpiper et al., 2009).

#### 5.4 Inflammatory markers

In hyperlipidemic patients a reduction was founded in CRP levels (28% vs. baseline) following a whole diet approach, which was low in saturated fat and included viscous fibers, almonds, soy protein, and plant sterols being comparable to statin therapy (33% reduction of CRP levels) and independent of changes in body weight. The diet also induced a reduction in lipids that was comparable to lovastatin therapy (Jenkins et al., 2003). They reported reduced CRP levels in hyperlipidemic patients consuming a high carbohydrate diet rich in viscous fiber-containing foods. However, the diets were also high in nuts (almonds), plant sterols and soy proteins, and it was therefore impossible to disentangle separate effects.

Kasim-Karakas et al. (2006) found that when carbohydrates replaced a substantial proportion of dietary fat under eucaloric conditions in post-menopausal women, the levels of several inflammatory markers increased along with an increase in triglycerides. However, when the participants consumed the 15% fat diet *ad libitum* under free living conditions, they lost weight and triglyceride and the levels of inflammatory markers decreased. In another study, Estruch et al. (2009) analyzed 772 cardiovascular high-risk subjects

concluding that plasma concentrations of CRP decreased in parallel with increasing DF ( $P=0.04$ ).

A review of seven clinical trials of at least 2 weeks in duration, with an increased and measurable consumption of DF, reported significantly lower CRP concentrations of 25-54% with increased DF consumption with dosages ranging between 3.3-7.8 g/MJ. The seventh trial with *Psyllium* fiber supplementation failed to lower CRP levels significantly in overweight/obese individuals. Weight loss and altered fatty acid intakes were present in most of the studies (North et al., 2009). The mechanisms are inconclusive but may involve the effect of DF on weight loss, and/or changes in the secretion, turnover or metabolism of insulin, glucose, adiponectin, interleukin-6, free fatty acids and triglycerides.

## 6. Conclusions

Based on epidemiological and clinical studies that have attributed important health effects to fiber, several organizations such as the American Dietetic Association and the Institute of Medicine recommend an intake of 14 g of DF per 1,000 kcal, or 25 g/day for adult women and 38 g/day for adult men, to protect against the risk of CHD and T2DM and improved weight maintenance. However, in most Western countries, the current intakes of DF are below those recommended with, for instance, an average consumption of 19 and 16 g per day for men and women, respectively. In order to improve the DF intake of the population, national dietary guidelines usually recommend the consumption of high-fiber foods.

Since no biomarker of DF intake is available, food frequency questionnaire (FFQ) data is the only source of information on food consumption, including DF. FFQs are known to contain measurement errors, a reason why energy intake should be included as a covariate in the models to achieve the equivalent of an isoenergetic diet and thereby overcome this problem.

The evidence available shows that the intake of foods that are high in fiber has clear benefits regarding lipid profile and other cardiovascular risk factors. Although some studies of fiber supplements have shown positive effects on the lipid profile, the number of adults who adhere to the use of fiber supplements tends to be low. Likewise, these effects are modest when compared with a whole foods approach that encourages the consumption of fiber-rich foods.

Epidemiologic studies show that intact fruit, vegetables, whole grains, nuts and legumes, all of which are rich in potentially cardioprotective components, protect the body from cardiovascular diseases and mortality. There is debate in relation to cereals that are especially rich in insoluble fiber, but some studies have shown an inverse association between their intake and blood pressure. However, in clinical studies, only soluble viscous fiber has been demonstrated to have metabolic advantages. This paradox can be explained by the fact that food rich in fiber contains other phytochemical compounds that have been demonstrated to modulate inflammation, oxidation, insulin resistance and cholesterol metabolism.

Consequently, a Mediterranean-style diet rich in fiber-rich foods should be recommended to reduce the risk of cardiovascular disease.

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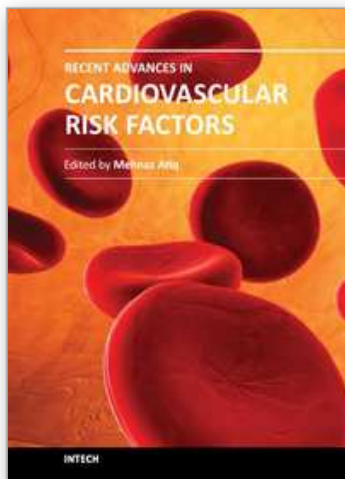
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Among the non-communicable diseases, cardiovascular disorders are the leading cause of morbidity and mortality in both the developed and the developing countries. The spectrum of risk factors is wide and their understanding is imperative to prevent the first and recurrent episodes of myocardial infarction, stroke or peripheral vascular disease which may prove fatal or disabling. This book has tried to present an update on risk factors incorporating new research which has thrown more light on the existing knowledge. It has also tried to highlight regional diversity addressing such issues. It will hopefully be resourceful to the cardiologists, general practitioners, family physicians, researchers, graduate students committed to cardiovascular risk prevention.

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