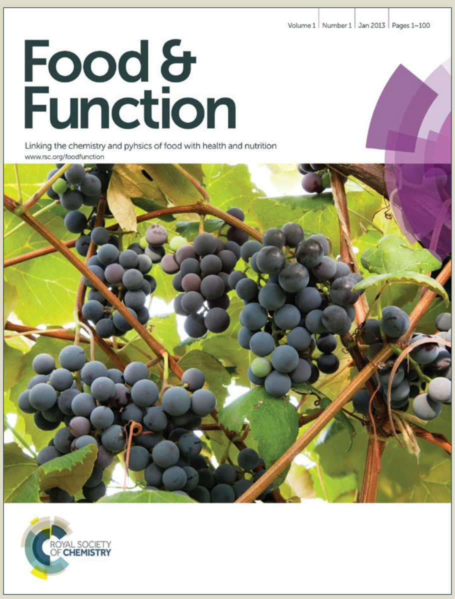
Food & Function

Accepted Manuscript



Dietary fiber and blood pressure control

Aleixandre A[1] and Miguel M[2*],

[1]Department of Pharmacology, Faculty of Medicine, Complutense University of Madrid, Avda. Complutense s/n, 28040 Madrid, Spain. [2] Institute of Food Science Research, (CSIC-UAM, CEI UAM+CSIC), Nicolás Cabrera, 9 28049, Madrid, Spain.

Short title: Fiber and blood pressure

Key words: Hypertension, dietary fiber, blood pressure

***Author for correspondence:**

Dr. Marta Miguel

Instituto de Investigación en Ciencias de Alimentación

C/ Nicolás Cabrera, 9, 28049 Madrid, Spain

Tel: + 34 91 0017931 Fax + 34 91 0017905

e-mail: marta.miguel@csic.es

Abstract

In the past years, new strategies to control blood pressure levels are emerging by developing new bioactive components of foods. Fiber has been linked to the prevention of a number of cardiovascular diseases and disorders. β-glucan, the main soluble fiber component in oat grains, was initially linked to a reduction in plasma cholesterol. Several studies have shown afterward that dietary fiber may also improve glycaemia, insulin resistance and weight loss. The effect of dietary fiber on arterial blood pressure has been the subject of far fewer studies than its effect on the above-mentioned variables, but research has already shown that fiber intake can decrease arterial blood pressure in hypertensive rats. Moreover, certain fibers can improve arterial blood pressure when administered to hypertensive and pre-hypertensive subjects. The present review summarizes all those studies which attempt to establish the antihypertensive effects of dietary fiber, as well as its effect on other cardiovascular risk factors.

Introduction

Blood pressure is the force of blood pushing against the walls of the arteries as the heart pumps blood. Thus, blood pressure is determined both by the amount of blood the heart pumps and by the amount of resistance to blood flow in the arteries. Therefore, blood pressure is expressed by two measurements, the systolic (SBP) and diastolic (DBP) pressures, which are the maximum and minimum pressures, respectively, in the arterial system. The SBP occurs when the left ventricle is most contracted, and the DBP occurs when the left ventricle is most relaxed prior to the next contraction. Normal blood pressure at rest is within the range of 100–140 millimeters mercury (mm Hg) SBP and 60–90 mm Hg DBP. In any case, the more blood the heart pumps and the narrower the arteries, the higher the blood pressure, and when the long-term force of the blood against the artery walls is high enough that it may eventually cause health problems, we can consider that a condition of high blood pressure or hypertension exists. Hypertension is actually present if the resting blood pressure is persistently at or above 140/90 mm Hg for most adults; different numbers apply to children. See Table 1.

It is possible to have hypertension for years without any symptoms but, even without symptoms, damage to blood vessels and heart continues. Uncontrolled high blood pressure increases in fact the risk of serious health problems such as coronary artery disease, stroke, aortic aneurysm, peripheral artery disease, and chronic kidney disease. On the other hand, modern lifestyle factors such as physical inactivity, salt-rich diets with processed and fatty foods, and alcohol and tobacco use, are responsible for a growing burden of hypertension, and this pathology affects millions of people around the world.

Nevertheless, this pathology is the most common modifiable risk factor for cardiovascular disease and death, and fortunately it can be easily detected and effectively treated nowadays. Thus, lowering blood pressure with antihypertensive drugs may reduce target organ damage and prevents cardiovascular disease outcomes. However, many people unknown their hypertensive condition or shows high arterial blood pressure values because of an inadequate or discontinued medical treatment. Moreover, despite of available treatment options, there are still patients whose hypertension is very difficult to control with current drugs, thus motivating further research in this field.[1]

Functional foods are natural or processed foods that contain known biologically-active compounds which provide a clinically proven and documented health benefit, and thus, an important source in the prevention, management and treatment of chronic diseases. Functional foods deliver therefore additional or enhanced benefits over and above their basic nutritional value. In the past two decades, new strategies for controlling blood pressure are emerging by developing new bioactive components of foods. The corresponding functional foods may provide new therapeutic applications for hypertension prevention and treatment, and contribute to a healthy cardiovascular population.[2] In this context, we can mention that numerous studies have revealed the cardiovascular benefits of consuming dietary fiber. [3,4]

Fiber is the name given to a group of compounds, found in foods of plant origin (cereals, fruit, vegetables and pulses), which are resistant to degradation by human digestive enzymes.[5,6] As regards to water solubility, dietary fiber may be subdivided into non-soluble and soluble fiber. As its name suggests, non-soluble fiber is made up of water insoluble substances (cellulose, hemicellulose, lignin and resistant starch). These components resist the action of intestinal microorganisms; so we can consider this type of fiber to be non-fermentable. On the contrary, soluble fiber is made up of components which are both water soluble and gel-forming (inulin, pectin, gums and fructooligosaccharides) and which give volume to faeces. These substances, found mainly in pulses, cereals (oat and barley) and certain fruits, are used by intestinal microorganisms, particularly colon flora. This kind of fiber is therefore known as fermentable fiber. The greatest degree of fermentation takes place in the caecum and in the ascendant colon. Figure 1 shows the capacity of some components of dietary fiber to ferment in the colon.

Health properties of dietary fiber

In 1974, Barkitt et al established a link between fiber consumption and the prevention of various diseases and disorders.[7] In fact, the beneficial effect of dietary fiber on the cardiovascular system has been known for some time, and it has been suggested that dietary fiber supplementation could be used to improve the metabolic syndrome and related risk factors, such as hypercholesterolemia, hypertriglyceridemia, hyperglycemia, body weight and appetite. In the present section we shall analyse the effect of fiber on these disorders since dietary fiber may benefit hypertension through the control of all them[8].

For a considerable number of years, oat has been one of the most closely studied fiber-rich foods. In 1963, De Groot et al. were the first to publish a paper on the beneficial cardiovascular effect of including oat in the diet. De Groot's team proposed that when oat was added to the diet, blood cholesterol levels were reduced. They replaced the bread fed by 21 men by oat-enriched bread. After 3 weeks, it was observed that plasma cholesterol levels of those participating in the study had dropped by 11%.[9] Later on, Wood concluded that β-glucan was the main soluble fiber component present in oat grains. In fact, this researcher indicated that β-glucan was responsible for the beneficial effects on health of this fiber.[10] Since the publication of De Groot's study in 1963, many other pieces of research have linked administration of oat β-glucan to a decrease in cholesterol. In 1992, Ripsin et al. [11], and afterward, in 1999, Brown et al.[12] reviewed the existing scientific information regarding the link between oat consumption and cholesterol. These researchers concluded that a daily intake of 3 g of soluble fiber reduced blood cholesterol by 5.9 mg/dl in people who did not have high cholesterol levels. This intake in turn caused a decrease of 18.6 mg/dl in people with initially high cholesterol levels.

In 1997, the American *Food and Drug Administration* (FDA) approved the registration of oat bran as a primary food in cholesterol reduction. Moreover, this organization established a set of guidelines to regulate the use of claims about unrefined oat and their derivatives in labelling. The guidelines also regulated the use of claims about the soluble fiber contained in this food. On January 21st

1997, the "health claim" consisting in "a diet high in soluble fiber and low in saturated fats and cholesterol may reduce the risk of heart disease" was accepted. After reviewing 37 studies, it was concluded that, in order to significantly reduce cholesterol levels, it should be consumed at least 3 g of oat β-glucan daily [13]. Moreover, from this time many intervention studies have highlighted the cholesterol lowering properties that we have mentioned for this dietary fiber.[14-18] The hypocholesterolemic effects of fibers other than oat, such as *Psyllium* (fiber from the *Plantago ovata* plant, specifically from the husks of the plant's seed) [19-21], guar gum (type of fiber also called guaran, that is a galactomannan. It is primarily the ground endosperm of guar beans. The guar seeds are dehusked, milled and screened to obtain the guar gum)[21] and pectin (heteropolysaccharide contained in the primary cell walls of plants)[22,23], and several pulses[23,24], have also been demonstrated.

Fermentation of soluble fiber in the colon results in the final production of gases (methane, carbon dioxide, and hydrogen) and short-chain fatty acids (acetate, propionate, butyrate, and valerate) that produce local and systemic effects. These fatty acids are organic acids with 2–5 carbons. Acetate is the acid produced in the greatest quantity, followed by propionate. Both short chain fatty acids, acetate and propionate, pass to the liver via the portal vein, and we would like to emphasize that both have an effect on the hepatic regulation of the metabolism of lipids, including cholesterol.

In addition, fiber intake may also improve weight loss[24-26], glycaemia and insulin resistance[27-30.] Obesity is a highly significant cardiovascular risk factor, and fiber-rich foods usually have a low energy content. Thus fiber consumption constitutes a calorie-dilution mechanism. Foods rich in fiber need in addition to be chewed longer and, as a result, more saliva is produced, leading to an increase in the time taken to eat the food and in the feeling of satiety. It is important to note that the effects of dietary fiber may be related to different gut hormones, which regulate satiety, energy intake, and/or pancreatic functions[31].

Moreover, in the intestine, the incorporation of fiber may complicate the union between digestive enzymes and their substrate, thus slowing down the absorption of nutrients. Soluble fiber attenuates, in particular, the speed of carbohydrate absorption, lowering the postprandial glycemic and insulinemic responses. During digestion, wave-like currents caused by contractions of the intestinal muscles bring nutrients to the surface of the intestinal wall for absorption. After soluble fiber dissolves in water, however, it traps nutrients inside its gummy gel and slows down considerably whilemoving through the digestive tract. Inside the gel, nutrients are shielded from digestive enzymes and less likely to reach the wall of the intestines. In fact, dietary fiber may retard enzyme access to starch and may impede bulk diffusion of the products of luminal digestion to the mucosal surface. It is also true that in order for nutrients to be absorbed into the intestines, they must first cross an unstirred water layer covering the surface of the intestines, and soluble fiber thickens this layer, making it more resistant to the movement of nutrients diffusing into the body. This explains why blood glucose levels rise more slowly when consumed with soluble fiber. In conclusion, dietary fiber converts the small intestine into a storage organ for the slow release of glucose to the portal circulation and, consequently, sugar is absorbed into the blood stream more slowly, blunting the sharp spike in blood glucose typically experienced by diabetic patients after a meal. Fewer spikes in blood glucose, in turn, lead to greater sensitivity to the action of insulin[31].

Despite the undeniable beneficial effects of dietary fiber on the related cardiovascular risk factors, with special importance for this review is that the studies described below also demonstrate the beneficial effects of some kinds of fibers on arterial blood pressure.

Dietary fiber and arterial blood pressure

Far fewer studies have been made on the possible effects of fiber on arterial blood pressure, than have been carried out until now on its effects on other cardiovascular risk factors. However, the study *Dietary Approaches to Stop Hypertension* (DASH) already indicated that diets high in fiber and low in salt and fat decreased arterial blood pressure[32]. Later on, several experimental studies in adequate animal models, and some other studies in hypertensive and prehypertensive patients, have also shown the beneficial effects of different kind of fiber on the control of arterial blood pressure. All this will be discussed below.

Animal studies

The effect of dietary fiber on arterial blood pressure of laboratory animals began only to be studied following the discovery of its beneficial effect on other variables, but some recent studies, that show the beneficial effects of certain fibers on the arterial blood pressure of rats, are particularly worthy of mention. In 1998 Obata and colleagues found that the husk of *Psyllium* seeds, a fiber which improves glycaemia and lipid profile, also reduced arterial blood pressure in stroke-prone spontaneously hypertensive rats (SP-SHR) fed an increased salt diet. These researchers carried out a study using 4 groups of 6 week-old SP-SHR rats, each group receiving one of the following diets: standard, enriched with 3% *Psyllium,* enriched with 10% *Psyllium* and enriched with 10% cellulose. All the groups ingested 0.05% salt in their drinking water for a month. At the end of this period, the animals fed the *Psyllium* enriched diet showed a significant decrease in arterial blood pressure when compared with those fed the standard or the cellulose enriched diet. The *Psyllium* enriched diet also caused a decrease in the left ventricle weight of the SP-SHR rats and lowered in addition the sodium-potassium relationship in these animals' faeces. [33] Some years later, Li and colleagues carried out a study on Goto-Kakizaki rats, an animal model of type 2 *mellitus* diabetes. These researchers divided the Goto-Kakizaki rats into 3 groups, which were fed for 16 weeks three different diets, containing rye, white rice and corn starch, respectively. The rats' arterial blood pressure was measured every 4 weeks. The rye diet significantly decreased, from the 12 week of treatment, SBP. This diet lowered also plasma total cholesterol, plasma triglycerides and cholesterol associated with low-density lipoproteins (LDL cholesterol), in the animals. These researchers concluded that fiber intake could have beneficial effects on arterial blood pressure and blood lipids. They suggested diets containing fiber for patients with diabetes *mellitus* in order to prevent complications associated with this disease.[34] The following year, Galisteo and his team also carried out a study with obese Zucker rats fed for 25 weeks a fiber enriched diet containing 3.5% *Plantago ovata*. These researchers determined different variables in the animals, and also performed experiments with acetylcholine in the aorta rings of the rats which had ingested *Plantago ovata,* in order to evaluate possible changes in endothelial function caused by this fiber. They showed that consumption of *Plantago ovata* prevented endothelial dysfunction, hypertension and the development of obesity in the Zucker rats. The study also revealed that this fiber improved dyslipidaemia, as well as abnormal concentrations of adiponectin and tumour necrosis factor-α (TNF-α).[35] Our research group also demonstrated the beneficial effects of dietary fiber on arterial blood pressure of Zucker fatty rats[36] and spontaneously hypertensive rats (SHR). More precisely, we demonstrated that the addition of 0.75 g a day of a soluble cocoa fiber product, to the drinking water, made it possible to attenuate the onset of hypertension in the SHR. When the administration of this product was stopped and the rats started to drink plain water, they regained arterial blood pressure levels similar to those of the control group, which had drunk only water during the whole period[37]. More recently, we could confirm again that the short-term administration of a soluble cocoa fiber product decreased SBP in the SHR (unpublished results).

The underlying antihypertensive mechanisms of dietary fiber have not been elucidated. Insulin resistance is implicated in the development of hypertension[38] and it has been reported that soluble fibers may affect blood pressure by modulating insulin metabolism.[39] Reductions in plasma cholesterol levels are also associated with improvements in endothelium-mediated vasodilation and blood pressure reduction.[40-42] The weight loss that dietary fiber causes has also been suggested as a potential mechanism to decrease high blood pressure levels.[43-45] More recently, the effects of oat wholemeal or β-glucan on insulin sensitivity and energy metabolism of rats has been investigated. The referred study demonstrated that oat β-glucan increases ATPase activity and energy charge in the small intestine of rats, improving insulin sensitivity and benefiting intestinal health[46]. However, more studies are needed in order to fully elucidate the mechanisms involved in the beneficial effects of dietary fibers against high blood pressure and related disorders.

Human studies

Some years after the hypocholesterolemic effect of oat in humans was established, studies began to determine the effect of this kind of fiber on arterial blood pressure. In 2001 Saltzman et al. studied the effect of a hypocaloric diet containing oat fiber on hypertension, dyslipidaemia and excess weight. They could observe that an oat rich diet did not significantly reduce body weight in the men and women included in the study, but this diet did cause a decrease in SBP, without altering DBP. Moreover, this diet also lowered total cholesterol as well as LDL cholesterol. Moreover the benefits obtained with the oat rich hypocaloric diet on SBP and the lipid profile, were greater than those produced by the consumption of a hypocaloric diet containing no oat[25]. Subsequently, in 2002, Keenan et al. observed that the arterial blood pressure of a group of 18 untreated hypertensive patients, men and women, presenting slight hypertension values or considered prehypertensive (SBP = 130-160 mm Hg, DBP = 80-100 mm Hg, and at least one measurement greater than 140-90 mm Hg), decreased upon a 6-week-administration period of an oat β-glucan enriched diet. A standardized daily intake of 5.5 g β-glucan was maintained for this period. SBP and DBP decreased by 7.5 mm Hg and by 5.5 mm Hg, respectively, in these subjects, but in the control group, which consumed less than 1 g a day of fiber, there were no changes in either SBP or DBP. The patients consuming the oat β-glucan enriched diet also showed a tendency towards insulin sensitivity improvement, and, as would be expected, a significant reduction in total cholesterol (9%) and LDL cholesterol (14%).[47] The same year, it was discovered that the daily consumption of unrefined oat cereal supplements, could reduce the need for antihypertensive medication and improves arterial blood pressure figures in treated hypertensive patients presenting basal arterial blood pressure measurements of less than 160-100 mm Hg.[48] The study carried out by Davy and colleagues in 2002 was not however able to show that oat consumption lowered arterial blood pressure in hypertensive subjects.[49] Nevertheless, in 2004, He et al. once again demonstrated the beneficial effects of soluble oat fiber on a group of hypertensive patients with grade 1 hypertension. These patients were given soluble oat fiber for 12 weeks, and this fiber caused a significant decrease in SBP and DBP (3.4 mm Hg and 3.2 mm Hg, respectively) [50]. A meta-analysis published a year later concluded that an increase in dietary fiber was able to reduce arterial blood pressure in hypertensive patients.[51]

Fibers other than oat β-glucan have also shown to affect arterial blood pressure. In 2001, Burke and his team proposed that high levels of arterial blood pressure might be linked in general to low protein intake, and probably also to a low fiber intake. These researchers showed that a diet high in soya protein and *Psyllium,* caused a decrease in arterial blood pressure in a group of hypertensive patients receiving antihypertensive treatment. The effects of protein and fiber demonstrated to be cumulative, and decreases in SBP of 5 mm Hg were obtained when both were administered together.[52] Moreover, in 2002, Jenkins et al. established that the intake of certain fibers, like β-glucan or *Psyllium,* could produce small decreases in arterial blood pressure in hyperlipidaemic patients with normal arterial blood pressure values.[53] Mention should also be made of the study carried out by Pérez-Jiménez and colleagues in 2008 on 34 non-smoking adults who were given 7.5 g a day of a grape antioxidant fiber product for 16 weeks. This product contained 5.3 g of grape fiber and 1400 mg of polyphenols. The control group was composed of 9 non-smoking subjects who ingested a standard diet for the same period of time. The grape antioxidant fiber caused a significant decrease in total cholesterol (9%) and LDL cholesterol (9%), and also lowered SBP and DBP (6% and 5% respectively). An even greater reduction in total cholesterol (14.2%) and LDL cholesterol (11.6%) was obtained in hypercholesterolemic patients fed with this fiber. These researchers concluded that the effects of the studied product were greater than those of other fibers, like oat or *Psyllium,* because the grape antioxidant fiber also contained several polyphenol-type antioxidant components.[54] Solà et al., in 2010, demonstrated the antihypertensive effects of *Plantago ovata* husks in mild moderate hypercholesterolemic individuals[23] but Pal et al., in 2012, described only transient effects on blood pressure caused by *Psyllium* fibre supplementation on obese individuals.[55] Recently, it has been also demonstrated that the consumption of a cocoa product derived from cocoa husk, also containing fiber and polyphenols, produced hypotensive, hypoglycaemic and antioxidant effects in moderately hypercholesterolemic humans.[56]

Lee et al. (2009) carried out a study with a lupin flour enriched bread, a novel food with an ingredient naturally high in protein and fiber, and they observed that the ingestion of this diet reduced SBP by 3 mm Hg in overweight men and women who had SBP and DBP values lower than 150 mm Hg and 95 mm Hg, respectively.[57] Moreover, it has been also suggested that the replacement of dietary carbohydrates by protein- and fiber-enriched foods might reduce arterial blood pressure.[58] Very recently, a systematic review and meta-analysis of the effect of dietary fiber type on blood pressure has been published. This review concluded that diets rich in β-glucans reduce SBP by 2.9 mm Hg, and DBP by 1.5 mm Hg. In addition, heterogeneity for individual fiber types was generally low. [59]

Table 2 summarizes the results obtained from 1998 until now, in different studies that have evaluated the effect of dietary fiber consumption on arterial blood pressure.

Conclusions

Dietary fiber has been linked to different cardiovascular benefits. β-Glucan and other soluble fiber components have been proposed to have in particular hypocholesterolemic effect, but fiber can also improve glycaemia, insulin resistance, triglyceride levels and weight loss. The effect of dietary fiber on arterial blood pressure has been also investigated. It is true that several studies indicate a relationship between dietary fiber and decreased arterial blood pressure values, but the controversy about the possible antihypertensive effect of dietary fiber remains debatable and the underlying mechanism remains to be clarified. This effect could probably be a consequence of the improved cardiovascular condition that follows long-term fiber consumption. Moreover, the particular components of some fibers could explain their antihypertensive effects. In any case, a direct effect of fiber on arterial blood pressure cannot be discarded, but seems quite difficult to prove, since only some fiber products have demonstrated short-term antihypertensive effects.

Table 1. Classification of hypertension according the seventh report of the Joint National Committee on the prevention, detection, evaluation, and treatment of high blood pressure

Classification	**Systolic blood pressure (mm Hg)**	**Diastolic blood pressure (mm Hg)**
Normal	<120	<80
Pre-hypertension	120-139	80-89
Stage 1 Hypertension	140-159	90-99
Stage 2 Hypertension	≥160	≥100

Table 2. Results obtained from 1998 in different studies which evaluate the effect of dietary fiber intake on blood pressure.

Type of fiber	Animals	Humans	Effect	References
Psyllium seed husk	Stroke-Prone spontaneously hypertensive rats		↓MAP	*33*
Oat		Normotensive	↓SBP (6 mm Hg)	*25*
Psyllium and soy protein		Hypertensive	↓SBP (5 mm Hg)	*52*
Oat		Hypertensive	No changes on BP	*49*
β-glucan and *Psyllium*		Normotensive	↓MAP	*53*
β-glucan from oat		Pre-hypertensive	↓SBP (7.5 mm Hg), ↓DBP (5.5 mm Hg)	*47*
Unrefined oat cereals		Hypertensive	↓MAP	*48*
Arabinogalactan		Healthy	No changes on BP	*60*
Oat		Normotensive	↓SBP (3.4 mm Hg), ↓DBP (3.2 mm Hg)	*50*
Barley	Goto-Kakizaki rats		↓SBP	*34*
Psyllium	Zucker fatty rats		↓MAP	*35*
Various types of fiber		Normotensive	↓MAP	*51*
β-glucan from oat		Hypertensive	↓SBP (8.3 mm Hg), ↓DBP (3.9 mm Hg)	*61*
Soluble fiber		Overweight and obese	↓SBP	*62*
β-glucan from barley		Hypercholesterolemic	No changes on BP	*63*
Grape antioxidant fiber		Normotensive	↓SBP (6%), ↓DBP (5%)	*54*
Lupin kernel		Pre-hypertensive	↓SBP (3 mm Hg)	*57*
Soluble cocoa fiber	Spontaneously hypertensive rats		↓SBP, ↓DBP	*37*
Soluble cocoa fiber	Zucker fatty rats		↓SBP, ↓DBP	*36*
Psyllium		Normotensive	↓ night-time SBP (3.1 mm Hg)	*64*
Fructans		Healthy	No changes on BP	*65*
Soluble cocoa fiber		Hypercholesterolemic	↓SBP, ↓DBP	*56*
Opuntia ficus-indica		Overweight and obese	No changes on BP	*66*
Glucomanan		Abdominal obese	No changes on BP	*67*

BP = blood pressure; SBP = systolic blood pressure; DBP = diastolic blood pressure; MAP = mean arterial pressure

Acknowledgments

This work was supported by MINECO, AGL2012-32387.

Literature cited

1. Oparil S, Schmieder RE. New approaches in the treatment of hypertension. *Circ Res*. 2015, **13**, 116.
2. Huang WY, Davidge ST, Wu J. Bioactive natural constituents from food sources-potential use in hypertension prevention and treatment. *Cri Rev Food Sci Nutr* 2013, **53**, 615-630.
3. Satija A, Hu FB. Cardiovascular benefits of dietary fiber. *Curr Atheroscler Rep* 2012, **314**, 505-514.
4. Bernstein AM, Titgemeier B, Kirkpatrick K, Golubic M, Roizen MF. Major cereal grain fibers and psyllium in relation to cardiovascular health. *Nutrients* 2013, **29**, 1471-1487.
5. De Vries JW, Prosky L, Li B, Cho S. A historical perspective of defining dietary fiber. *Cerea Foods World* 1999, **44**, 367-369.
6. Dietary Fiber Definition Committee of the American Association of Cereal Chemists, 2001.
7. Barkitt DP, Walker AR, Painter NS. Dietary fiber and disease. *JAMA* 1974, **229**, 1068-1074.
8. Hartley L, May MD, Loveman E, Colquitt JL, Rees K. Dietary fibre for the prevention of cardiovascular disease. *Cochrane Database Syst Rev*, 2016, 1:C011472. Doi: 10.1002/14651858.CD011472).
9. De Groot P, Luyken R, Pikaar NA. Cholesterol-lowering effect of rolled oats. *Lancet* 1963, **2**, 303-304.

10. Wood PJ. Relationships between solution properties of cereal beta-glucans and physiological effects a review. *Trends Food Sci Technol* 2002, 13, 313-320.

11. Ripsin CM, Keenan JM, Jacobs DR, Elmer PJ, Welch RR, Van Horn L, Liu K, Turnbull WH, They FW, Kestin M, Hegsten M, Davidson DM, Davidson MH, Dugan LD, Demark-Wahnfried W, Belings S. Oat products and lipid lowering. *J Am Med Associ* 1992, **267**, 3317-3325.

12. Brown L, Rosner B, Willett WW, Sacks FM. Cholesterol-lowering effects of dietary fiber: a meta-analysis. *Am J Clin Nutr* 1999, **69**, 30-42.

13. FDA. Food Labeling: Health Claims; Oats and Coronary Heart Disease. Food and Drug Administration (FDA). 1997, **62**, 3584-3601.

14. Kerckhoffs DA, Hornstra G, Mensink RP. Cholesterol-lowering effect of beta-glucan from oat bran in mildly hypercholesterolemic subjects may decrease when beta-glucan is incorporated into bread and cookies. *Am J Clin Nutr* 2003, **78**, 221-227.

15. Queenan KM, Stewar ML, Smith KN, Thomas W, Fulcher RG, Slavin JL. Concentrated oat beta-glucan, a fermentable fiber, lowers serum cholesterol in hypercholesterolemic adults in a randomised controlled trial. *Nutr J* 2007, **26**, 6.

16. Rondanelli M, Opizzi A, Monteferrario F, Klersy C, Cazzola R, Cestaro B. Beta-glucan- or rice bran-enriched foods: a comparative crossover clinical trial on lipidic pattern in mildly hypercholesterolemic men. *Eur J Clin Nutr* 2011, **65**, 864-871.

17. Tiwari U, Cummins E. Meta-analysis of the effect of beta-glucan intake on blood cholesterol and glucose levels. *Nutrition.* 2011, **27**, 1008-1016.

18. Lipsky H, Gloger M, Frishman WH. Dietary fiber for reducing blood cholesterol. *J Clin Pharmacol* 1990, **30**, 699-703.

19. Chan EK, Schroeder DJ. Psyllium in hypercholesterolemia. *Ann Pharmacother* 1995, **29**, 625-627.

20. Vuksan V, Jenkins AL, Rogovik AL, Fairgrieve CD, Jovanovski E, Leiter LA. Viscosity rather than quantity of dietary fibre predicts cholesterol-lowering effect in healthy individuals. *Br J Nutr* 2011, **31**, 1-4.

21. Solá R, Bruckert E, Valls RM, Narejos S, Luque X, Castro-Cabezas M, Doménech G, Torres F, Heras M, Farrés X, Vaquer JV, Martínez JM, Amaraz MC, Anguera A. Soluble fibre (Plantago ovata husk) reduces plasma low-density lipoprotein (LDL) cholesterol, triglycerides, insulin, oxidised LDL and systolic blood pressure in hypercholesterolaemic patients: a randomised trial. *Atherosclerosis* 2010, **211**, 360-367.

22. Knopp RH, Superko HR, Davidson M, Insull W, Dujovne CA, Kwitervich PO, Zavoral JH, Graham K, O´Connor RR, Edelman DA. Long-term blood cholesterol-lowering effects of a dietary fiber supplement. *Am J Prev Med* 1999, **17**, 18-23.

23. Escudero Álvarez E, González Sánchez P. La fibra dietética. *Nutr Hosp* 2006 **21**, 61-72.

24. Babio N, Balanza R, Basulto J, Bulló M, Salas-Salvadó J. Dietary fibre: influence on body weight, glucemic control and plasma cholesterol profile. *Nutr Hosp* 2010, **25**, 327-340.

25. Saltzman E, Krupa D, Lichtenstein AH, Dallal GE, Corrales A, Schaefer EJ, Greenberg AS, Roberts SB. An oat-containing hypocaloric diet reduces

systolic blood pressure and improves lipid profile beyond effects of weight loss un men and women. *J Nutr* 2001, **131**, 1465-1470.

26. Anderson JW, Baird P, Davis RH Jr, Ferreri S, Knudtson M, Koraym A, Waters V, Williams CL. Health benefits of dietary fiber. *Nutr Rev* 2009, **67**, 188-205.
27. Jang Y, Lee JH, Kim OY, Park HY, Lee SY. Consumption of whole grain and legume powder reduces insulin demand, lipid peroxidation, and plasma homocisteine concentrations in patients with coronary artery disease: randomised controlled clinical trial. *Arterioscler Thromb Vasc Biol* 2001, 21, 2065-2071.
28. Aller R, de Luis, AD, Izaola O, La Calle F, del Olmo L, Fernández L, Arranza T, Hernández JMG. Effect of soluble fiber intake en lipid and glucose levels en healthy subjects: A randomised Clinical Trial. *Diabetes Res Clin* 2004, **65**, 7-11.
29. Jenkins AL, Kacinik V, Lyon M, Wolever TM. 2010. Effect of adding the novel fiber, PGX®, to commonly consumed foods on glycemic response, glycemic index and GRIP: a simple and effective strategy for reducing post prandial blood glucose levels--a randomized, controlled trial. *Nutr J* 2010, **9**, 58.
30. Willis HJ, Thomas W, Eldridge AL, Harkness L, Green H, Slavin JL. Glucose and insulin do not decrease in a dose-dependent manner after increasing doses of mixed fibers that are consumed in muffins for breakfast. *Nutr Res* 2011, **31**, 42-7.
31. Aleixandre MA, Miguel M. Dietary fiber in the prevention and treatment of metabolic syndrome; A review. *Critical Rev Food ScI Nutr* 2008, **48,** 905-12-

32. Sacks FM, Obarzanek E, Windhauser MM, Svetkey LP, Vollmer WM, McCullough M, Karanja N, Lin PH, Stelle P, Proschan M, Evans MA, Appel LJ, Bray GA, Voght TM, Moore TJ for DASH investigators. Rationale and design of the Dietary Approaches to Stop Hypertension Trial (DASH). *Ann Epidemiol* 1995, **5**, 108-118.

33. Obata K, Ikeda K, Yamasaki M, Yamori Y. Dietary fiber, Psyllium, attenuates salt-accelerated hypertension in stroke-prone spontaneously hypertensive rats. *J Hypertens* 1998, 16, 1959-1964.

34. Li J, Wang J, Kaneko T, Qin LQ, Sato A. Effects of fiber intake on the blood pressure, lipid, and heart rate in Goto Kakizaki rats. *Nutrition* 2004, **20**, 1003-1007.

35. Galisteo M, Sánchez M, Vera R, González M, Anguera A, Duarte J, Zarzuelo A. A diet supplemented with husks of Plantago ovata reduces the development of endothelial dysfunction, hypertension, and obesity by affecting adeponectin and TNF-alpha in obese Zucker rats. *J Nutr* 2005, **135***,* 2399-2404.

36. Sánchez D, Moulay L, Muguerza B, Quiñones M, Miguel M, Aleixandre A. Effect of a soluble cocoa fiber-enriched diet in Zucker fatty rats. *J Med Food*, 2010,**13**, 621-8.

37. Sánchez D, Quiñones M, Moulay L, Muguerza B, Miguel M, Aleixandre A. Changes in arterial blood pressure of a soluble cocoa fiber product in spontaneously hypertensive rats. *J Agric Food Chem* 2010, **58**, 1493-1501.

38. Ferrannini E, Buzzigoli G, Bonadonna R. 1987. Insulin resistance in essential hypertension. *The New Eng J Med* 1987, **317**, 350–357.

39. Ferri C, Bellini C, Desideri G, Valenti M, De Mattia G, Santucci A, Hollenberg NK, Williams GH. Relationship between insulin resistance and nonmodulating hypertension: linkage of metabolic abnormalities and cardiovascular risk. *Diabetes*, 1999, **48**, 1623–1630.

40. Anderson TJ, Meredith IT, Yeung AC, Frei B, Selwyn AP, Ganz P. The effect of cholesterol-lowering and antioxidant therapy on endothelium-dependent coronary vasomotion," *The New Eng J Med* 1995, **332**, 488–493.

41. Vogel RA, Corretti MC, Plotnick GD. Changes in flow-mediated brachial artery vasoactivity with lowering of desirable cholesterol levels in healthy middle-aged men. *Am J Cardiol* 1996, **77**, 37–40.

42. Crago MS, West SD, Hoeprich KD, Michaelis K, McKenzie J. Effects of hyperlipidemia on blood pressure and coronary blood flow in swine. *FASEB J*. 1998, **12**, A238.

43. Neter JE, Stam BE, Kok FJ, Grobbee DE, Geleijnse JM. Influence of weight reduction on blood pressure: a meta-analysis of randomized controlled trials. *Hypertension* 2003, **42**, 878–884.

44. Howarth NC, Saltzman E, Roberts SB. Dietary fiber and weight regulation. *Nutr Rev* 2001 59, 129–139.

45. Slavin JL. Dietary fiber and body weight. *Nutrition* 2005, 21, 411-418.

46. Zhang PP, Hu XZ, Zhen HM, Xu C, Fan MT. Oat b-glucan increased ATPases activity and energy charge in small intestine of rats. *J Agric Food Chem* 2012, **60**, 9822-9827

47. Keenan JM, Pins JJ, Frazel C, Moran A, Turnquist L. Oat ingestion reduces systolic and diastolic blood pressure in patients with mild or borderline hypertension: a pilot trial. *J Fam Pract* 2002, **51**, 369.

48. Pins JJ, Geleva D, Keenan JM, Frazel C, O'Connor PJ, Cherney LM. Do whole-grain oat cereals reduce the need for antihypertensive medications and improve blood pressure control? *J Fam Pract* 2002, **51**, 353-359.

49. Davy BM, Melby CL, Beske SD, Ho RC, Dvrath LR, Davy KP. Oat consumption does not affect resting casual and ambulatory 24-h arterial blood pressure in men with high-normal blood pressure to stage I hypertension. *J Nutr* 2002, **132**, 394-398.

50. He J, Streiffer RH, Whelton PK. Effect of dietary fiber supplementation on blood pressure: A randomised, double-blind Placebo-controlled trial. *J Hypertens* 2004, **22**, 73-80.

51. Whelton SP, Hyre AD, Pedersen B, Yi Y, Whelton PK, He J. Effect of dietary fiber intake on blood pressure: a meta-analysis of randomised controlled clinical trials. *J Hypertens* 2005, 23, 475-481.

52. Burke V, Hodgson JM, Beilin LJ, Giangiulioi N, Rogers P, Puddey IB. Dietary protein and soluble fiber reduce ambulatory blood pressure in treated hypertensive. *Hypertension* 2001, **38**, 821-826.

53. Jenkins DJ, Kendall CW, Vuksan V, Vidgen E, Parker T, Faulkner D, Mehling CC, Garsetti M, Testolin G, Cunnane SC, Ryan MA, Corey PN. Soluble fiber intake at a dose approved by the US Food and Drug Administration for a claim of health benefits: serum lipid risk factors for cardiovascular disease assessed in randomised controlled crossover trial. *Am J Clin Nutr* 2002, **75**, 834-839.

54. Pérez-Jiménez J, Serrano J, Tabernero M, Arranz S, Díaz-Rubio E, García-Díez L, Goñi I, Saura-Calixto F. Effects of grape antioxidant fiber in cardiovascular disease risk factors. *Nutrition* 2008, **24**, 646-653.

55. Pal S, Radavelli-Bagatini S. Effects of psyllium on metabolic syndrome risk factors. *Obes Rev* 2012, **13**, 1034-1047.

56. Sarriá B, Mateos R, Sierra-Cinos JL, Goya L, García-Diz L, Bravo L. Hypotensive, hypoglycaemic and antioxidant effects of consuming a cocoa product in moderately hypercholesterolemic humans. *Food Funct* 2012, **3**, 867-874.

57. Lee YP, Mori TA, Puddey IB, Sipsas S, Ackland TR, Beilin LJ, Hodgson JM. Effects of lupin kernel flour-enriched bread on blood pressure: a controlled intervention study. *Am J Clin Nutr* 2009, **89,** 766-772.

58. Belski R. Fiber, protein, and lupin-enriched foods: role for improving cardiovascular health. *Adv Food Nutr Res* 2012, **66**, 147-215.

59. Evans CEL, Greenwood DC, Treapleton DE, Cleghorn CL, Nykjaer C, Woodhead CE, Gale CP, Burley VJ. Effects of dietary fibre type on blood pressure: a systematic review and metanalysis of randomized controlled trals of healthy individuals. *J Hypertens* 2015, **33**, 897-911.

60. Marett R, Slavin JL. No long-term benefits of supplementation with arabinogalactan on serum lipids and glucose. *J Am Diet Assoc,* 2004, **104,** 636–9.

61. Maki KC, Galant R, Samuel P, Tesser J, Witchger MS, Ribaya-Mercado JD, et al. Effects of consuming foods containing oat beta-glucan on blood pressure, carbohydrate metabolism and biomarkers of oxidative stress in men and women with elevated blood pressure. *Eur J Clin Nutr* 2007, **61**, 786–95.

62. Wood RJ, Fernandez ML, Sharman MJ, Silvestre R, Greene CM, Zern TL, et al. Effects of a carbohydrate-restricted diet with and without supplemental

soluble fiber on plasma low-density lipoprotein cholesterol and other clinical markers of cardiovascular risk. *Metabolism* 2007, **56**, 58–67.

63. Smith KN, Queenan KM, Thomas W, Fulcher RG, Slavin JL. Physiological effects of concentrated barley beta-glucan in mildly hypercholesterolemic adults. *J Am Coll Nutr* 2008, **27**, 434–40.

64. de Bock M, Derraik JG, Brennan CM, Biggs JB, Smith GC, CameronSmith D, et al. Psyllium supplementation in adolescents improves fat distribution & lipid profile: a randomized, participant-blinded, placebo-controlled, crossover trial. *PLoS One* 2012, **7**, e41735.

65. Niv E, Shapira Y, Akiva I, Rokhkind E, Naor E, Arbiv M, et al. Effect of levan supplement in orange juice on weight, gastrointestinal symptoms and metabolic profile of healthy subjects: results of an 8-week clinical trial. *Nutrients* 2012, **4**, 638–47.

66. Grube B, Chong PW, Lau KZ, Orzechowski HD. A natural fiber complex reduces body weight in the overweight and obese: a double-blind, randomized, placebo-controlled study. *Obesity (Silver Spring)* 2013, **21**:58–64.

67. Reimer RA, Yamaguchi H, Eller LK, Lyon MR, Gahler RJ, Kacinik V, et al. Changes in visceral adiposity and serum cholesterol with a novel viscous polysaccharide in Japanese adults with abdominal obesity. *Can J Diabetes* 2013, **37**, S246.

Figure 1. Water solubility and capacity to ferment in the colon of some components of dietary fiber