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Revisión

Effect of beta-glucans in the control of blood glucose levels of diabetic patients: a systematic review

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Abstract

Introduction: Functional foods have been widely utilized to reduce the symptoms of various diseases such as diabetes mellitus (DM). Among the foods used to combat these effects are soluble fibres, mainly those rich in beta-glucans (BGs).

Objective: To review the effects of beta-glucans (BGs) on glucose plasmatic levels of diabetic individuals.

Design: A search was conducted using the Pubmed, Science Direct and Scielo databases using the keywords: diabetes mellitus and beta-glucan and glucose and glycaemia. As inclusion criteria, only studies on diabetic human individuals (type 1 or type 2) who consumed BGs were selected.

Results and Discussion: Of the 819 initial articles retrieved, only 10 fit the inclusion criteria and were used in the study. It was observed that doses around 6.0g/person/day, for at least 4 weeks were sufficient to provoke improvements in the blood glucose levels and also lipid parameters of individuals with DM. However, glucose levels do not reach normal levels using BG alone. Low doses of BG for at least 12 weeks were also reported to promote metabolic benefits.

Conclusions: Based on previous research, it was concluded that the ingestion of BGs was efficient in decreasing glucose levels of diabetic patients. The consumption of greater doses or smaller doses for longer periods of time produced better results.

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Key words: *Metabolic syndrome*. *Diabetes* Mellitus. *Polysaccharides*. *Glucans*. *Barley*

EFECTO DE LOS BETA-GLUCANOS EN EL CONTROL DE LOS NIVELES DE GLUCOSA EN PACIENTES DIABÉTICOS: REVISIÓN SISTEMÁTICA

Resumen

Introducción: Alimentos funcionales han sido ampliamente utilizados para reducir los síntomas de diversas enfermedades como la diabetes mellitus (DM). Entre los alimentos utilizados en el combate de estos efectos, están las fibras solubles, principalmente aquellas que tienen buena cantidad de beta-glucano (BG's).

Objetivo: El objetivo de esta revisión sistemática fue evaluar los efectos de los BG´s en los parámetros metabólicos de individuos diabéticos.

Métodos: Fue conducida una búsqueda en las bases de datos Pubmed, ScienceDirect y cielo, utilizando las siguientes palabras-clave: diabetes mellitus and beta-glucano and glucosa and glucemia. Como criterio de inclusión, fueron seleccionados solamente estudios en individuos diabéticos (tipo 1 o tipo 2) que consumieron BG´s.

Resultados y Discusión: De los 819 trabajos inicialmente encontrados, 10 artículos se encuadraron en los criterios de inclusión, y por eso fueran utilizados en el estudio. Fue observado que dosis superiores de 6,0 g/individuo/día, o dosis más grandes que 3,0 g/individuo/día por un periodo de tiempo más largo, son suficientes para provocar mejoras en los parámetros glucémicos y lipidicos de portadores de DM. Bajas dosis de BG por al menos 12 semanas también presentaron efectos metabólicos benéficos.

Conclusión: Tomando en cuenta los resultados observados, se concluye que los BG´s son eficientes en la atenuación de los efectos indeseables del DM, siendo las dosis más grandes o el consumo de pequeñas cantidades por un tiempo más largo las que promueven resultados mejores.

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Palabras-clave: *Síndrome metabólico*. *Diabetes* Mellitus. *Polisacáridos*. *Glucanos*. *Avena*.

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Introduction

Diabetes mellitus (DM) is a metabolic disorder caused by a deficiency in producing insulin or inefficient action of this hormone, which leads to chronic hyperglycaemia and other disorders such as vascular alterations, myocardic infarction, nephropathies, retinopathies, and neuropathies[1]. It is estimated that 5% of all deaths worldwide are resulted from diabetes complications[2], and by the year of 2030 there will be more than 366 millions of diabetic people in the world[3].

Conventional treatment of diabetes involves the use of insulin or hypoglycemic agents[4]. However, frequently the use of medications is expensive and involves side effects[5]. As a result, various researchers have investigated non-pharmacological forms of treatment, such as physical activity[6,7] and functional foods[8,9], in order to prevent and mitigate the harmful effects of diabetes.

The ingestion of foods with a low glycaemic index is a helpful alternative in controlling diabetes[10]. Important among these foods are those rich in fibre, especially those with a high level of beta-glucans[11]. Beta-glucans (BGs) are non-starch polysaccharides present in grains like oats, rye and barley, as well as mushrooms, yeast and some grasses[12,13]. Studies have suggested that foods containing BGs have anti-diabetic effects[8,10,11]. These fibres seem to form a barrier in the small intestine which prevents glucose and other nutrients absorption, reducing consequently the glycaemia, insulinaemia[14] and also cholesterol serum levels[12]. Furthermore, it is hypothesized that BGs may act in activating metabolic pathways through PI3K/Akt, which plays a key role in the pathogenesis of diabetes[15].

Studies assessing the effects of BGs in individuals who are likely to develop metabolic syndrome are frequent[16-18], but the evidence of consuming these fibres to improve glycaemia, HbA1c, insulin levels and lipid profile in individuals with type 1 or 2 DM is not well established.

Therefore, considering the potential of BGs in attenuating the negative effects of DM, the objective of this systematic review was to evaluate the effects of this type of fibre on blood glucose control of diabetic individuals.

Design

Research Strategy

In November 2013 we conducted an electronic search on the Pubmed database (http://www.ncbi.nlm.nih.gov) using the following keywords: diabetes mellitus and beta-glucan, beta-glucan and glycaemia, diabetes mellitus and beta-glucan, and beta-glucan and glucose. To confirm the results and obtain complementary studies, a similar methodology was utilized in the ScienceDirect (http://www.sciencedirect.com) and Scielo databases (http://www.scielo.org/php/index.php), using the same keywords in English.

Selection of Studies

We selected studies which used BGs in the diets of individuals with type 1 or type 2 DM. We opted to select only studies that were conducted on humans with *diabetes mellitus*. There were no restrictions on the way in which the BGs were introduced into the diet, whether mixed into other foods or administered in their pure form. Furthermore, there were no restrictions on the dosage used, experimental period, sample size, language and/or date when the article was published.

Three researchers conducted the searches separately so that later the selected studies could be checked for conformity with the inclusion criteria. In cases of deviation among the selected items, all of the criteria were reviewed and discussed.

Quality Criteria

Quality criteria were adapted from other systematic reviews[19,20] and in the instrument proposed by Jadad[21]. The adopted parameters were:

Randomized studies: experiments where the diets or the groups were randomized received a score of 2, while non-randomized experiments, or studies in which this fact was not clearly described in the text, received a score of 1.

Blind evaluation: Double or single blind studies received a score of 2, while articles without blind evaluations, or where this fact was not clearly described in the text, received a score of 1.

Control group: papers which related the use of control group, whether in the form of a control diet or a control group of individuals (non-diabetic individuals) received a score of 2, and those which did not report the use of a control group or did not clearly cite this in the text received a score of 1.

Placebo: studies using placebo diets received a score of 2, and studies which did not use or did not clearly describe use of placebos received a score of 1.

Questions about dietary habits: articles which described the use of a questionnaire or interview with a nutritionist received a score of 2, while those which did not describe the use of a questionnaire received a 1.

Additional variables: articles which evaluated only glycaemia and/or glycosylated haemoglobin (HbA1c) and insulin levels received a score of 1; those which evaluated further variables such as total cholesterol, LDL-c, HDL-c, apolipoproteins, PPAR-γ, etc. received a score of 2 (Table I).

Tabla I
Scores for evaluation criteria

Authors	*A*	*B*	*C*	*D*	*E*	*F*	*Total*
Cugnet-Anceau et al.[8]	2	2	2	2	2	2	12
Liatis et al.[12]	2	2	2	1	1	2	10
Reyna et al.[14]	2	1	2	1	2	2	10
Kabir et al.[10]	2	1	1	1	2	2	9
Pick et al.[28]	2	1	2	1	1	2	9
Jenkins et al.[11]	2	1	1	1	2	1	8
Braaten et al.[23]	1	1	2	1	2	1	8
Tapola et al.[27]	2	1	2	1	1	1	8
Rami et al.[22]	2	1	1	1	1	1	7
Tappy et al.[26]	1	1	2	1	1	1	7

(A) Randomized studies: 2 points; non-randomized studies: 1 point. (B) Blind evaluation: 2 points; absence of blind evaluation: 1 point. (C) Control group: 2 points; absence of control group: 1 point. (D) Use of placebos: 2 points; lack of placebos: 1 point. (E) Questionnaires about dietary habits: 2 points; non-use of questionnaires: 1 point. (F) Analysis of glycaemia and/or HbA1c and insulin levels: 1point; additional variables such as total cholesterol, LDL-c, HDL-c, apolipoproteins, PPAR-γ, etc.: 2points.

According to the adopted criteria, the maximum possible score was 12 points. Other parameters such as age, sex, experimental period, dose of BGs, and type of diabetes, among others, did not earn points but were used for descriptive purposes in order to contribute to the discussion.

Results

The bibliographic survey conducted on PubMed database yielded 151 articles, and 10 of these were chosen for this review. The search using the ScienceDirect database yielded 668 articles. However, no additional articles were selected. Scielo database search did not retrieve any article. Therefore, 10 articles were used in this review (Figure 1).

Out of the selected articles, 9 (90.0%) used only individuals with type 2 DM in their samples. In all studies, the age of the study participants varied from 11 to 66 years, and the minimum sample number was eight volunteers, while the maximum was 53. In 70% of the studies, interviews were conducted by nutritionists to evaluate participants' dietary profiles before and du-

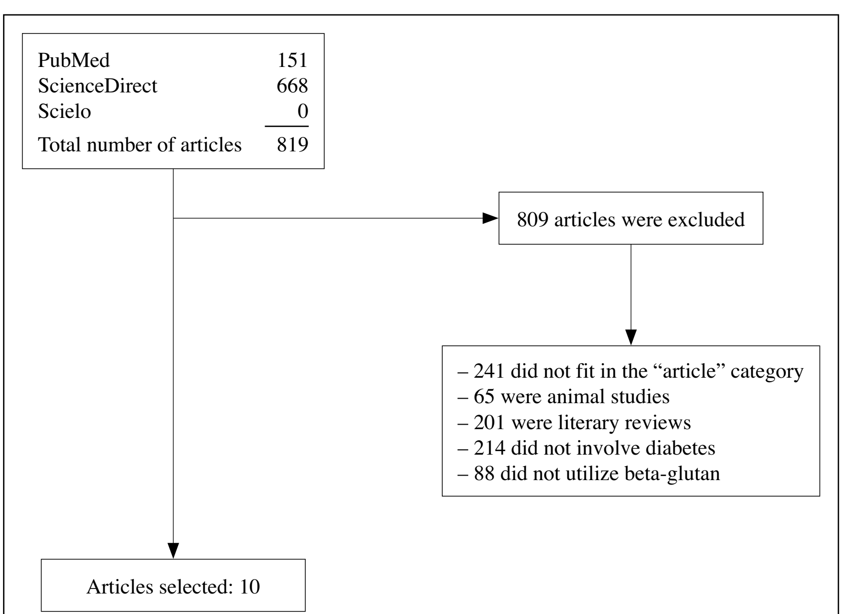

Fig. 1.—Flowchart of the article search process using the keywords "diabetes mellitus" and "beta-glucan" and "glycaemia" and "glucose" and "human".

ring the experimental period. The most common methodological difficulties were blinding and the use of placebo diet.

As for use of BGs in the diet, the minimal dose described was 1.8 g/person/day[22], while the maximum was 9.4 g/person/day[23], and in all the studies the BGs were derived from oats. The experimental meals with BGs were consumed in different formulations; the majority of them were in the form of breakfast cereals or baked goods (Table II). In 50% of the studies the experimental meals were consumed in the morning, 10% at lunch or dinner, and in 30% of the studies the time of consumption was not stipulated or not described. The parameters which were frequently assessed were glycaemia, HbA1c, total cholesterol, HDL, and LDL. Insulin levels were evaluated in 30% of the articles. The principal methodological characteristics of the selected articles are presented in Table II.

Discussion

Systematic reviews generally use pre-defined methods to conduct a wide bibliographic study in order to allow the definition of an evidence of a modality of treatment for a specific disease. The present review was conducted to determine the effectiveness of BGs in reducing blood glucose levels in patients with DM, as well as to determine the most effective dose needed to obtain these results. In order to avoid excluding any articles, a careful review was conducted by the authors. Nevertheless, due to variations in the titles, indexing, and keywords, it is possible that some articles may not have appeared in the results.

Despite the fact that articles existed which studied the efficacy of fibre in mitigating the effects of diabetes[24,25], for the present study we selected only articles which mentioned specific quantities of BGs. We also stress that the criteria which evaluated methodological quality were defined based on previous studies[19-21] and the authors' experiences. Controlled blind randomized studies receive high scores because of their methodological quality and level of evidence. According to the results of the present review, doses of BGs below 3.5 g/person/day were not significant in reducing glycaemia[2,8] and glycosylated haemoglobin[10] in diabetic individuals. This finding corroborates previous report from the European Food Safety Authority[26] stating that the claim of reduction of post-prandial glycaemic response may be used only for food which contains at least 4 g of beta-glucans from oats or barley for each 30 g of available carbohydrates in a quantified portion as part of the meal. However, the present results suggested that doses above 6.0 g/person/day were more efficient to reduce glycaemia and insulinaemia[27,28]. Moreover, the duration of consumption was a determining factor in the efficacy of this substance against these parameters. A 12-week period of daily ingestion of a dose of 3.0 g/person provoked a 46% reduction of

Tabla II
Summary of the selected studies

Author and year of publication	*Control group*	*Average age of participants and type of DM.*	*N*	*Experimental period*	*Dose of beta-glucans*	*Parameters assessed*	*Principal effects of BGs*
Braaten et al. [23]	Yes	55 years, with type 2 DM.	21 CG: 7 men and 4 women EG: 7 men and 3 women.	Three sessions of one dose with an interval of at least 3 days between sessions.	8.8g in oatmeal porridge.	Glycaemia and insulin.	↓ postprandial PG and PI.
Cugnet-Anceau et al. [8]	Yes	62 years, with type 2 DM.	53 CG: 24 EG: 29.	Adaptation (both groups): 3 weeks consuming soup without BGs. Experimental Phase: -experimental group: 8 weeks consuming soup with BGs. - control group: 8 weeks consuming soup without BGs.	3.5g in soup which was consumed once per day.	PG, HDL-c, LDL-c, total cholesterol, TG, Apo-B, HbA1c, C-reactive protein.	↓ TG

Tabla II (cont)
Summary of the selected studies

Author and year of publication	*Control group*	*Average age of participants and type of DM.*	*N*	*Experimental period*	*Dose of beta-glucans*	*Parameters assessed*	*Principal effects of BGs*
Jenkins et al. [11]	NC	61 years, with type 2 DM.	16 (10 men and six women)	Four weeks, consuming a test meal one time per week.	7.3g in 50 g breakfast cereal 6.2g in the form of a 50g cereal bar. 3.7g in 50g of oat bread.	GI, palatability.	↓ GI (> concentration of BGs= < GI).
Kabir et al. [10]	No	59 years, with type 2 DM.	13 men.	Two periods of four weeks with 15 days between.	3g in breakfast cereals and breads.	PG, PI, HDL-c, LDL-c, total cholesterol, TG, free fatty acids, Apo AI and Apo-B, HbA1c, Peroxisome Proliferator- activated Receptor γ (PPARγ), leptin, and CETP mRNAs.	↓ PG peak, total cholesterol, Apo-B. ↑ quantity of RNA-m for leptin in abdominal adipose tissue.
Liatis et al. [12]	Yes	63 years, with type 2 DM.	41 volunteers. CG: 11 men and seven women. GE: 23 (12 men and 11 women).	Three weeks.	3g in bread.	PG, HbA1c, TG, HDL-c, LDL-c, total cholesterol, PI, Homeostasis model of assessment-insulin resistanse (Homa-IR).	↓ LDL-c, total cholesterol, fasting PI and and Homa-IR.
Pick et al. [28]	Yes	45 years, with type 2 DM.	Eight.	Two periods of 12 weeks.	3g in bread or other baked goods.	PI, fasting PG, HbA1c, total cholesterol and HDL-c.	↓ PG and IP curves, LDL-c and total cholesterol.
Rami et al. [22]	NC	11 years, with type 1 DM.	38 (18 boys and 20 girls).	12 nights.	1.8 g in biscuits or cereal bars.	PG and HbA1c.	No alterations
Reyna et al. [14]	Yes	50 years, with type 2 DM.	16 men	Four weeks.	5.4g in bread and 10g in a biscuit.	BMI, PI, HDL-c, LDL-c, total cholesterol, TG, HbA1c.	↓ BMI, PG, HbA1c. ↑ HDL
Tappy et al. [26]	Control meal.	56 years, with type 2 DM.	Eight (seven men and one woman).	Four separate days.	Four, six or 8.4g in breakfast cereals.	PG, PI, HbA1c.	↓ Postprandial PI. ↓ PG with ↑ dose of BGs.
Tapola et al. [27]	Control meal	66 years with type 2 DM.	12 (7 men and 5 women).	Five different days (glucose tolerance test on each day)	9.4 ; 4.6 and 3.0 g in glucose solutions.	Glucose tolerance test.	↓ Postprandial PG and PG peak.

Abbreviations: DM= Diabetes Mellitus; CG= Control Group; EG= Experimental Group; NC = not clear; PG= Plasma Glucose; PI= Plasma insulin; GI= Glycaemic Index; TG= Triglycerides; BMI= Body Mass Index. The evaluated variables which are not in the results column were not presented because they did not show significant differences.

glycaemia in relation to the control group[29], while the same dose ingested for four weeks[10] or 3.5 g/person/day for eight weeks were not effective[8]. A possible mechanism to explain the reduction of glycaemia through consumption of BGs is the fact that this substance creates a gelatinous layer in the intestine that reduces the absorption of carbohydrates by the enterocytes[14]. These fibers promote the formation of soluble viscous solutions which slow the gastric emptying rate decreasing digestion and absorption of nutrients. Thus, how higher the layer, lowest is the glucose uptake[30], and this fact explains why studies evaluating small dose did not show significant reduction in glucose blood level. In addition, short-chain fatty acids resulting from the anaerobic bacterial fermentation of BG's in the colon may be related to the maintenance of glucose and insulin balance[31]. It is also reported in experiments using rats that short chain fatty acids, such as acetate, proprionate and butyrate can enhance the expression of GLUT-4 via PPAR gamma in muscle fibers and adipocytes, increasing glucose uptake and consequently decreasing blood glucose[31].

The influence of fibrous foods with elevated doses of BGs on reducing fasting hypoglycaemia episodes were also reported in the literature[32]. Doses of 8.8 g/person modulated the increase of insulin and glycaemia in the first 40 minutes of the glycaemic test in individuals with type 2 DM, while for 150 and 180 minutes, this dosage caused glucose levels to remain higher in comparison with the control group[27]. However, consumption of night-time snacks containing 1.8 grams of BGs did not produce effects on hypoglycaemia in children with type 1 DM[25]. Studies investigating the effects of consumption of BGs by human patients with DM type 1 are scarce. Only one study was retrieved in the present search based on the employed criteria.

The lack of studies evaluating the effectiveness of the use of BGs in humans with Type 1 DM-insulin dependent patients may be related to the fact that this type of fiber is often used in disorders where there is the presence of obesity[33,34] as is the case with type 2 diabetes[16,20]. However, some promising results were found in an animal model of type 1 diabetes, showing that there may be benefits on glycemic control, and improvement in antioxidant profile (upregulation of SOD and CAT in liver and kidney), which plays an essential role in alleviating oxidative stress accompanying diabetes[35]. Although it was not the main goal of the present research, it was found that for plasmatic lipoproteins, doses between 3.0 and 6.0 g/person/day for two to four weeks decreased levels of triglycerides[10], total cholesterol[12,14], LDL cholesterol[14], and also caused an increase in HDL-cholesterol[10,14] (Table II). Improved lipid profile due to consumption of BGs is related to the increase in the conversion of cholesterol into bile acids, which promotes the reduction of cholesterol levels in the enterohepatic circulation[36]. Another mechanism was shown by an *in vitro* study, where BGs inhibited the capture of long-chain fatty acids in intestinal tissue, principally when these substances were present in high concentrations[37].

Besides, it was observed that the consumption of BGs caused a decrease in body mass in individuals with type 2 diabetes (significant results were observed for ingestion of doses superior to 3g/person/day during a period of at least three weeks)[12,14]. Again, it is suggested that since the fibers cause increased viscosity of the chyme, it slows the gastric emptying, causing the individual to have a satiety feeling leading to the consumption of less energy[38]. Furthermore, it was found that doses between 4 and 6 grams of BG increased levels of pancreatic peptide hormone PYY[33]. This hormone is related to satiety and brain signaling of satisfaction, playing an important role in the control of obesity[39].

Another relevant factor to be considered is related to the physicochemical characteristics of this polysaccharide, such as molecular weight, chemical conformation, solubility, viscosity and positioning its ramifications[40]. With respect to the molecular weight, it is considered that BGs with high molecular weight such as those derived from oats have a higher viscosity, which provides additional health benefits (better glycemic control and levels of total cholesterol and LDL-c) compared to fibers with lower molecular weight[30]. Furthermore, it has been suggested that the functionality of BGs can be altered by their physical-chemical characteristics, whereas the conformation of polysaccharides ß -1,3/1,4 (usually present in the composition from oats) tend to have greater metabolic potential[41], while the conformation of ß -1,3/1,6 tend to have higher potential immunological[42]. However, both features play metabolic and immune activity[43,44].

With respect to the immunostimulatory function, it is suggested that high molecular weight BGs from fungi directly activate leukocytes while the lower molecular weight only modulate the response of cells previously stimulated by cytokines[45]. The stimulation of the immune response caused by BGs may be related to its binding on specific receptors that activate macrophages, which triggers various processes such as chemotaxis, macrophage migration, degranulation leading to increased expression of adhesive molecules and adhesion to the endothelium, in addition to increased activity of hydrolytic enzymes, signaling processes that activate other cells and secretion of cytokines[44]. Thus, the consumption of BGs by diabetic patients may play an important role not only for glucose homeostasis as well as on the immune system.

Conclusion

Based on the results observed in the studies which were evaluated in the present review, BGs can be considered effective substances in improving glycaemic and lipid control in individuals with type 2 DM, with higher doses or lower doses for longer periods providing better results. Out of the 10 studies retrieved, 9 reported metabolic benefits. The only studied which reported absence of effects was conducted in type 1 patients[22]. This fact was expected since as discussed above, most of the effects of BG are more prone in the intestine reducing carbohydrates absorption. However, the effects of these fibres on humans with type 1 DM were not widely studied. It must be considered that it is difficult to evaluate the effects of BGs on those individuals, since they are often dependent on exogen insulin. Thus, it is suggested that studies using adjunctive therapy in patients with diabetes, both type 1 and type 2 BGs associated with the use of other agents as modulators of glucose, for example, regular physical activity, hypoglycemic and even lower doses insulin. Additionally, due to the inexistence of longitudinal studies evaluating the consumption of these substances for years, it cannot be inferred that such consumption will not provoke deleterious effects.

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