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The role of yoghurt consumption in the management of type II diabetes

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Enrichment of yoghurt with specific ingrdients beneficially affects the management of Type II Diabetes Mellitus (DMII). As far as the role of yoghurt in the management of DMII is concerned, the limited number of randomized clinical trials (RCTs) which have been conducted suggest that daily intake of yoghurt enriched with vitamin D and/or calcium as well as probiotics positively influences glycemic regulation and may contribute to more effective control of the disease. It is argued that the various ingredients which are already contained in the complex matrix of food, such as bioactive peptides, calcium, B-complex vitamins and beneficial microbes, as well as the fact that it can be used as a vehicle for the inclusion of other effective ingredients can have an impact on the metabolic control of diabetic patients. The aim of this review is to present the RCTs which have been conducted in the last decade in patients with DMII in an attempt to highlight the positive effects of yoghurt in the management of the disease.

Introduction

Type II diabetes mellitus (DMII) is a chronic noncommunicable disease, which is a scourge of the modern age and degrades the quality of life of the sufferers. The contemporary lifestyle which is characterized by oversupply/overconsumption of food, decreased physical activity and intense stress results in the constant increase in the occurrence of the disease. According to the World Health Organization (WHO), diabetes is among the ten main causes of death worldwide and in 2016, it led to the death of approximately 1.6 million people.[1] Taking measures and developing strategies are of utmost importance both for the prevention and correct management of diabetes. Besides medication, changes in lifestyle is an integral part of preventing or/and managing the disease.

Numerous research studies that have been carried out support that a lifestyle characterized by a balanced diet and increased physical activity may act preventively against the development of diabetes and have a beneficial effect on diabetic patients, impeding or retarding the progression of the disease and the occurrence of complications. Among these studies are dietary interventions, which have focused on specific food groups, some of which are milk and other dairy products, particularly yoghurt.[2,3]

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Yoghurt is a product of high nutritional value and a rich source of nutrients like proteins, vitamins and minerals as well as beneficial microbes. It is believed that these ingredients can have an impact on the intestinal microbiota and contribute to the prevention and management of diabetes even though their mechanisms of action have not been fully clarified.[4] However, a lack of several nutrients has been observed in diabetic patients due to the disease, medication or/and other factors. Therefore, it is considered that the inclusion of yoghurt in their daily dietary pattern may improve the nutritional status of these subjects and contribute to better metabolic control. In recent years, there have been studies on various functional foods, whose bioactive compounds may be able to improve the function of β-pancreatic cells, the secretion of insulin, insulin resistance and hyperglycemia, and to regulate the metabolism of lipids and in this way, contribute to the prevention of the occurrence of macrovascular and microvascular complications of diabetes.[5] These products also include dairy products, which either contain or can be enriched with bioactive ingredients, which may act beneficially for the management of the disease. Such ingredients are calcium, B vitamins, several bioactive peptides, conjugated linoleic acid and lactic acid bacteria. The following is a report of the clinical studies in which the effect of consumption of yoghurt on the metabolic control of patients with DMII was examined.

Medline and Scopus databases were searched for RCTs conducted in patients with DMII who followed dietary intervention with yoghurt using relevant indexing terms as "yoghurt", "yogurt", "type II diabetes", "glycemic control", "vitamins", "probiotics", and "randomized clinical trials". The search included articles published from 2010 until May 26, 2020. Titles were reviewed by two independent researchers. References of the identified articles were also examined for appropriate studies that were missed. There were no restrictions in terms of participants' characteristics. Dates of publication for the summary table are referred to 2010 onward and only studies on humans published in English language papers were eligible (Table 1).

Yoghurt: nutritional value and benefits for human health

Yoghurt is a remarkable source of nutrients for the human body and its systematic consumption can offer a series of health benefits.[4] It is a product of milk fermentation and contains microorganisms which can beneficially affect host metabolism. Lactose is the main carbohydrate in this product, which due to the presence of lactic acid bacteria, is more tolerable to people with lactose intolerance compared to that contained in milk. Specifically, yoghurt can be better tolerated due to the presence of β-galactosidase, which is either included or produced by bacteria in the small intestine helping in the digestion of lactose. Furthermore, yoghurt is a significant source of proteins of high biological value, and as a product of bacterial fermentation, supplies the body with microorganisms beneficial to the intestine (probiotics).[6] Among the valuable nutrients that the consumption of yoghurt provides, are various vitamins such as vitamin A, vitamin D (in enriched yoghurt), riboflavin, folic acid, B12, and minerals, like calcium, phosphorus, zinc and magnesium.[7,8] Although it generally contains nutrients similar to those of milk from which it has been produced, it has higher concentrations of these ingredients.[9]

The fermentation process not only makes milk more digestible, but also increases its shelf life and its microbiological safety. More specifically, the lactic acid bacteria which are included in fermented dairy products, and therefore in yoghurt too, are able to inhibit the survival and development of various pathogenic bacteria in humans, like *Escherichia* and *Salmonella enteritidis*. Lactic acid, produced by fermentation, reduces pH and it appears that it delays the development of unwanted microorganisms.[4] Thus, it has been suggested that the consumption of yoghurt is a shield against infections and inflammations of the gastrointestinal system and the live bacteria that yoghurt contains hinder colonization and multiplication of pathogenic bacteria, which are transmitted to humans through food consumption. It is also worth mentioning that yoghurt and other dairy products that have undergone fermentation may contain more folic acid than milk from which they are made, since this vitamin is a product of synthesis of specific strains of lactic acid bacteria.[10]

In a recent meta-analysis of studies on the effects of the consumption of dairy products in the prevention of the occurrence of various types of cancer, the intake of fermented dairy products was associated with a reduction in the danger of the occurrence of the disease.[11] Furthermore, in some studies the consumption of yoghurt showed a protective effect against various forms of cancer, like bladder cancer[12] and colon cancer.[13] Additionally, a recent systematic review of studies and meta-analysis presented an inverse relationship between the intake of yoghurt and the development of the metabolic syndrome.[14] In a meta-analysis of 14 clinical trials it was noted that the consumption of milk which had undergone fermentation had positive effects on the reduction of blood pressure in pre-hypertensive and hypertensive subjects,[15] while the high total intake of dairy products (5 portions per week against 1 portion per month) and particularly in the form of yoghurt, has been associated with a lower risk of occurrence of hypertension in middle-aged or older people.[16] However, a meta-analysis conducted in 2017 did not show any correlation between the consumption of yoghurt and the reduction of cardiovascular risk.[17] Furthermore, data from several meta-analyses support that the intake of yoghurt can contribute to the prevention of the development of DMII,[18–21] probably due to its effects on the control of body weight and on energy metabolism.[22–25] Finally, it is worth noting that the consumption of yoghurt has been associated with a healthier lifestyle. More specifically, various studies have shown a higher intake of nutrients as well as improved nutritional quality, which is characterized by higher consumption of fruits, vegetables, whole meal products and dairy products, in individuals who systematically consume yoghurt, in comparison to individuals who rarely or never consume yoghurt. Moreover, people who consume yoghurt often have other healthy habits too, such as exercising more and smoking less as they have higher awareness and knowledge of nutrition compared to non-consumers.[25]

Yoghurt consumption probably is a shield against the development of many chronic diseases. For this reason, in the past years researchers have focused on conducting dietary interventions aiming to elucidate the possible beneficial effects of this food on various diseases[26] among which DMII is included.

Yoghurt and glycemic control in type II diabetes mellitus

DMII is a chronic metabolic disease which is a problem in most of the countries in the world and concerns the modern scientific community, mainly due to the significant complications caused by its unsuccessful management.

According to the WHO it is estimated that approximately 422 million people all over the world suffer from diabetes while 1.6 million deaths annually are attributed to this disease. For this reason, several research studies have focused on nutritional interventions aiming at the prevention of the occurrence of DMII. Among these are the studies which investigate the effect of the consumption of dairy products. However, their findings are not clear, since there are studies that show a protective effect of the consumption of dairy products on the occurrence of DMII[2,3] while others do not

Table 1 Randomized clinical trials (RCTs) examining the effects of yoghurt on glycemic control of patients with DMII

Reference	Study design	Number of participants (total/final)	Age (years)	Control group	Intervention group	Effects on glycemic control
Shab-Bidar *et al.* (2011)[51]	Double-blind – 12 weeks	100/100	52.5 ± 7.4	2 × 250 mL d^{-1} conventional yoghurt drink (doogh) noVitD, 170 mg Ca/250 mL (*n* = 50)	2 × 250 mL d^{-1} yoghurt drink enriched with vitamin D3 (doogh), 170 mg Ca + 500 IU VitD/250 mL (*n* = 50)	Fasting glucose Fasting insulin HbA1c QUICKI
Nikooyeh *et al.* (2011)[40]	Double-blind – 12 weeks	90/90	50.7 ± 6.1	2 × 250 mL d^{-1} conventional yoghurt drink (doogh) without added VitD, 150 mg Ca/250 mL (*n* = 30)	2 × 250 mL d^{-1} yoghurt drink enriched with vitamin D3 (150 mg Ca + 500 IU VitD/250 mL) (*n* = 30) or 2 × 250 mL yoghurt drink enriched with vitamin D3 & Ca 250 mg Ca + 500 IU VitD/250 mL (*n* = 30)	Fasting glucose HbA1c HOMA-IR
Li and Xing *et al.* (2016)[52]	Double-blind – 16 weeks	137/103	28.7 ± 4.7	2 × 100 g d^{-1} conventional yoghurt drink without added VitD (*n* = 49)	2 × 100 g d^{-1} yoghurt enriched with 500 IU VitD (*n* = 48)	Fasting glucose Fasting insulin HOMA-IR
Jafari *et al.* (2016)[53]	Double-blind – 12 weeks	60/59	57.3 ± 5.6	100 g d^{-1} conventional yoghurt without added VitD (*n* = 29)	100 g d^{-1} yoghurt enriched with vitamin D 2000 IU VitD/100 g (*n* = 30)	Fasting insulin HOMA-IR QUICKI
Hajimohammadi *et al.* (2017)[54]	Single blind – 12 weeks	100/100	52.5 ± 7.4	2 × 250 mL d^{-1} conventional yoghurt 170 mg Ca without added VitD (*n* = 50)	2 × 250 mL d^{-1} yoghurt enriched with vitamin D 170 mg Ca, 500 IU VitD/250 mL (*n* = 50)	Fasting glucose QUICKI
Ejtahed *et al.* (2012)[75]	Double-blind – 6 weeks	64/60	50.9 ± 7.5	300 g d^{-1} conventional yoghurt	300 g d^{-1} yoghurt fortified with probiotics (*L. acidophilus* La5, *B. lactis* BB12)	Fasting glucose Insulin HbA1c
Mohamadshani *et al.* (2014)[76]	Double-blind – 8 weeks	44/42	51.0 ± 6.5	300 g d^{-1} conventional yoghurt (*n* = 21)	300 g d^{-1} yoghurt fortified with probiotics (*L. acidophilus* La5, *B. lactis* BB12) (*n* = 21)	Fasting glucose HbA1c
Hove *et al.* (2015)[77]	Double-blind – 12 weeks	46/41	59.6 ± 6.5	300 mL d^{-1} conventional yoghurt (*n* = 18)	300 mL d^{-1} milk fermented with *L. helveticus* (*n* = 23)	Fasting glucose
Ostadrahimi *et al.* (2015)[97]	Double-blind – 8 weeks	68/60	35–65	2 × 600 mL d^{-1} conventional yoghurt drink (doogh) (*n* = 30)	2 × 600 mL d^{-1} kefir with probiotics (*n* = 30)	Fasting glucose HbA1c
Rezaei *et al.* (2017)[80]	Double-blind – 4 weeks	90/90	50.3 ± 10	3 × 100 g d^{-1} conventional yoghurt (*n* = 45)	3 × 100 g d^{-1} yoghurt with probiotics (*n* = 45)	Fasting glucose HbA1c
Tonucci *et al.* (2017)[78]	Double-blind – 6 weeks	50/45	51.4 ± 6.9	120 g d^{-1} conventional fermented milk product (*n* = 22)	120 g d^{-1} conventional fermented milk product fortified with probiotics *L. acidophilus* La-5, *B. lactis* BB-12 (*n* = 23)	HbA1c
Hasaniani *et al.* (2019)[95]	Double-blind – 8 weeks	70/58	53.4 ± 5.7	200 g d^{-1} conventional yoghurt 2.5% without linseed (*n* = 28)	200 g d^{-1} yoghurt 2.5% with 30 g linseed (*n* = 29)	HbA1c
Yanni *et al.* (2019)[66]	Single-blind – 12 weeks	33/28	63.3 ± 1.7	2 × 200 g d^{-1} conventional yoghurt, 0% fat (*n* = 14)	2 × 200 g d^{-1} yoghurt, 0% fat dessert enriched with vitamins of the complex B (B1, B5, B6) (*n* = 14)	No significant effects on glycemic parameters Body weight reduction improvement of homocysteine levels

support any correlation.[27,28] Equally unclear are the results of the studies which have examined the relationship of specific dairy products with DMII. Based on current data the meta-analyses of several prospective studies point in the direction that the consumption of dairy products low in fat and of specific dairy products, such as cheese and yoghurt, is inversely correlated with the risk of occurrence of DMII. In contrast, there seems to be no relation between full-fat dairy products and DMII.[18,19]

Regarding the research on the effect of the intake of dairy products on diabetic patients, the number of RCTs that have been conducted is very limited. Actually, the studies related to yoghurt and to its effect on DMII are even fewer. Most of them have focused on a fermented dairy product, which is a yoghurt drink known as doogh, a traditional product of the Middle East. In general, it seems that the daily consumption of this drink by diabetic persons, particularly when it is enhanced with specific nutrients, could improve several parameters related to the glycemic control of these patients.[29]

The mechanism through which the consumption of yoghurt is connected with the prevention and possibly the management of DMII has not been fully clarified. The regular consumption of yoghurt seems to have a direct effect on the satiation or/and the distribution of energy, reducing fat, which is strongly connected with insulin resistance and the risk of DMII. The simplest interpretation of the effect of yoghurt consumption on energy intake is that the systematic consumption of healthy and nutrient dense foods, like yoghurt, in the long run, leads to the reduction of the consumption of less healthy foods, which are rich in fat, simple sugars and consequently in energy. Another interpretation of the effect of yoghurt on the reduction of energy intake is connected with specific nutrients present in this product, like proteins and calcium, which increase the feeling of satiety.[30–32] Proteins, vitamins and metals are more concentrated in yoghurt than in milk while low pH increases the bioavailability of calcium which has been suggested to facilitate weight and fat mass loss.[33,34] However, effects on the regulation of appetite hormones after long term consumption of conventional yoghurt without energy restriction has not been supported by clinical studies. Another mechanism concerns the direct effect of yoghurt intake on the protection of β-pancreatic cells, on insulin sensitivity and on the secretory function of the pancreas.[35] Various ingredients of yoghurt, like calcium, magnesium, vitamin D (in enriched yoghurt), proteins and lactic acid bacteria are believed to be involved in these mechanisms. Probiotic bacteria which exist in yoghurt and other fermented milk products can beneficially alter the gut microbiota population and affect host metabolism. Consumption of these foods delivers a large number of lactic acid bacteria which alter the intestinal environment, resulting in the reduction of lipopolysaccharide production and the increase of the tight junctions of the gut epithelial cells.[36] Microbial products and metabolites affect adipogenesis and insulin resistance while significant correlations have been discovered between specific intestinal bacteria, metabolic pathways and DMII.[36,37] Consumption of certain types of yoghurt can suppress endotoxin production and ameliorate endotoxemia and inflammation through the regulation of the immune system.[36,38] RCTs have shown that probiotic yoghurts are more effective than conventional yoghurts in the improvement of health outcomes such as blood glucose and antioxidant status in cases of DMII, insulin resistance, obesity and fatty liver disease.[39]

Yoghurt enriched with vitamin D or/and calcium

Lack of vitamin D is a common phenomenon observed on a large scale worldwide, both in healthy people and in people with underlying diseases.[40,41] Actually, it seems that diabetic patients have lower levels of vitamin D compared with healthy people.[42,43] The possible effect of vitamin D on DMII is indicated by a seasonal variation in the glycemic control in people with DMII, which deteriorates in winter, since during this period the frequency of hypovitaminosis D is greater.[44] The improvement of vitamin D levels in diabetic people probably improves insulin secretion[45,46] and reduces insulin resistance.[47] The effect of vitamin D on insulin secretion may be either direct, through its binding to vitamin receptors in β-pancreatic cells, or indirect, through the regulation of the extracellular calcium. Moreover, vitamin D seems to act against systematic inflammation, eliminating the cytokines produced by the body.[48]

Regarding calcium, it seems that it is involved in various processes related to glycemic control. Specifically, this mineral participates in the phosphorylation of insulin receptors, affects the secretory function of β-pancreatic cells and influences insulin resistance through the inhibition of gene regulators which encode pre-inflammatory cytokines.[49,50]

Based on the above data, in the past decade a number of clinical studies in DMII patients have been conducted, aiming to investigate whether the consumption of yoghurt enriched with vitamin D or/and calcium could have a beneficial effect on parameters related to the glycemic control of these patients.

In 2011, in a randomized double blind clinical trial, which was performed on 100 diabetic persons, the daily consumption of 500 mL yoghurt drink enriched with vitamin D and calcium (500 IU/250 mL, 170 mg) for 12 weeks improved the fasting glucose and fasting insulin as well as endothelial biomarkers compared to the conventional drink.[51] In the same year, in a study carried out in 90 diabetic patients, it was also found that the daily consumption of yoghurt drink enriched with vitamin D and calcium (500 IU/250 mL, 150 mg, 500 mL day^{-1}) for 12 weeks had a stronger effect on glycemic control compared to the conventional yoghurt drink.[40]

In a randomized double-blind clinical trial, women aged 24–31 with Gestational Diabetes Mellitus participated. For a 16-week time period they were consuming either a yoghurt drink enriched with vitamin D (500 IU, 2×100 g d^{-1}) or conventional yoghurt drink. The group of women who received the vitamin-enriched drink had a significantly greater improvement of the insulin and fasting glucose levels as well as of the lipid profile in relation to the group of women who received the conventional drink.[52] In a randomized double-blind clinical trial performed on 59 postmenopausal women with DMII, who consumed yoghurt enriched with vitamin D (2000 IU in 100 g d^{-1}) or conventional yoghurt for a period of 12 weeks, a significant improvement of glycemic parameters was observed, with the exception of glycosylated hemoglobin, in women who consumed the functional yoghurt in contrast to those who received the conventional yoghurt.[53]

One more randomized single-blind clinical trial was performed, in which 100 persons with DMII participated. The study lasted 12 weeks and included two groups. The first group consumed a vitamin D/Ca enriched yoghurt drink (170 mg Ca and 500 IU vitD/250 mL) twice a day, while the other one consumed with the same frequency and for the same time period a conventional yoghurt drink (170 mg Ca without vitD). This study proved an increase of leptin and ghrelin levels in the blood even though the fraction of leptin/ghrelin was decreased. In addition, this study supported that the improvement of vitamin D levels in people with DMII can have a positive effect on insulin sensitivity and on appetite hormones.[54]

Yoghurt enriched with B-complex vitamins

The chronic uncontrolled hyperglycemia observed in DMII can cause significant changes in the state of micronutrients in the body, and also these nutrients can have a direct effect on glucose homeostasis. Scientific studies on DMII patients show that deficiency of vitamins (particularly B-complex vitamins) and minerals is common in these patients. Apparently, in diabetic people, increased diuresis due to osmotic effects of high blood glucose can result in the faster removal of water-soluble B vitamins through the urine compared to people without diabetes, even if the intake is sufficient. More specifically, thiamine (B1), pyridoxine (B6) and biotin (B7) have been found in reduced concentrations in diabetic patients, however, the mechanisms causing this situation remaining unclear. Supplementation of these vitamins in DMII patients seems to lead to some improvement in metabolic control. Additionally, folic acid (B9) and cobalamin (B12) are the two vitamins found in insufficient quantities in the body of diabetic persons. The prolonged use of metformin which is the first drug of choice in diabetes seems to negatively affect the absorption of the above two vitamins. As a result, their levels appear reduced in diabetics and there is probably a need for their supplementary administration. As it is known, B vitamins play a key role in energy metabolism since they are involved in various complex chemical reactions that take place inside the cells. That is why it is desirable that they be maintained at normal levels in the body, particularly of diabetic subjects. Based on rat studies, lack of thiamine seems to cause acute disorders with respect to the composition and secretion of insulin by the pancreas.[55,56] Studies performed on diabetic individuals show that the supplementary administration of thiamine can have positive effects. For instance, in a randomized double-blind clinical trial, the administration of thiamine (150 mg d^{-1}) for one month led to the reduction of glucose and leptin levels in the diabetic group compared to the control group.[57] Furthermore, in another study, the supplementary administration of thiamine and pyridoxine for a period of five months to diabetic renal patients led to the reduction of increased DNA glycosylation in the leukocytes of these patients, and in this way helping towards the prevention of the development of diabetic complications.[58] Moreover, in a double-blind, controlled with placebo, study on diabetic patients with microalbuminuria, the oral administration of a high dose of thiamine supplement (3 × 100 mg d^{-1}) for three months resulted in the reduction of the renal excretion of albumin, proving in this way that this vitamin could reverse microalbuminuria in early stage nephropathy.[59]

Very few studies have examined the possible effect of supplementary administration of pantothenic acid (B5) in pathological conditions like diabetes. Specifically, they have investigated the use of pantethine in diabetic individuals for the improvement of cholesterol and triglyceride levels and obtained positive results without any negative effects.[60–62]

Similar to the studies concerning pantothenic acid, the studies which have examined the supplementary administration of vitamin B12 to diabetic individuals are very few. Specifically, in a study, the administration of pyridoxine supplement, folic acid and B12 to people with diabetic retinopathy led to the improvement of retinal edema and increased light sensitivity.[63] It is also worth mentioning that in a meta-analysis of seventeen studies it appeared that the supplementary administration of lipoic acid and methylcobalamin can improve the speed of transmission of nerve impulses and diabetic neuropathy.[64] Finally, in another study it appeared that diabetic individuals who were being treated with metformin showed reduced cognitive performance in comparison to individuals who did not receive metformin or were non-diabetic. Thus, some scientists claim that the use of vitamin B12 supplements in elderly diabetic patients who receive metformin probably has beneficial effects on their cognitive performance.[65]

Recently, in a 12-week clinical trial, the effect of the consumption of yoghurt enriched with B vitamins against conventional yoghurt on 33 overweight/obese individuals with DMII was investigated. Specifically, these individuals were randomly assigned to two groups. The first group consumed two servings of non-fat yoghurt enriched with B vitamins (B1, B5, B6) daily without energy restriction, while the other one received the same quantity of conventional non-fat yoghurt daily, also with no caloric restriction. At the end of 12 weeks the first group showed a significant improvement of the B vitamins status and homocysteine levels in the blood, reduction of energy consumption and body weight, without any change in glycemic parameters.[66] According to our knowledge there are no other studies in bibliography which examine the effect of yoghurt or other dairy products enriched with vitamin B on glycemic control of patients with DMII.

Yoghurt enriched with probiotics

Based on the definition by the WHO, probiotics are defined as "those living microorganisms which, when given in sufficient quantities, offer some benefit to the health of the host".[67] The benefits that probiotics offer to human health are multiple and refer primarily to the improvement of the function of the immune and gastrointestinal systems. Moreover, studies on animal models show a possible beneficial effect of probiotics on blood glucose levels probably by the reduction of inflammation and prevention of β-pancreatic cell destruction.[68] The mechanisms by which probiotics are involved in glucose metabolism have not been clarified. It is considered that the intake of probiotics protects the β-pancreatic cells against oxidative damage preventing peroxidation of lipids and increasing antioxidants like glutathione and peroxide dismutase.[69] Furthermore, it has been observed that probiotics influence inflammation and insulin resistance by the increase of natural killer cells and regulation of the expression of tumor necrosis factor-a (TNF-a).[70] Other possible mechanisms with impact on glucose metabolism are the increase of gliclazide bioavailability, the inhibition/delay of the intestinal glucose absorption, and alterations of the intestinal microbiome.[71–74]

In the last decade several RCTs have been performed aiming to investigate the effect of the consumption of yoghurt enriched with probiotics on the glycemic control of DMII patients.[75–78] More specifically, Ejtahed *et al.*, conducted a clinical trial aiming to investigate the possible effects of yoghurt enriched with probiotics against conventional yoghurt on diabetic patients. In their study they included 64 subjects who were divided into two groups. The intervention group consumed 300 g of yoghurt enriched with probiotics (*Lactobacillus acidophilus* La5 and *Bifidobacterium lactis* Bb12, 7.23×10^6 and 6.04×10^6 cfu g^{-1}, respectively) daily for 6 months, in contrast with the control group that for the same period consumed 300 g of conventional yoghurt daily. The results of the study showed a beneficial effect of probiotics on the fasting glucose and glycosylated hemoglobin in the intervention group against the control group.[75]

Another randomized clinical trial also studied the effect of yoghurt enriched with probiotics (*Lactobacillus acidophilus* La5 and *Bifidobacterium lactis* Bb12, 3.7×10^6 cfu g^{-1}) on 44 persons with DMII. This study had a similar dosage form to the aforementioned study by Ejtahed *et al.*, but the intervention lasted a shorter time period (8 weeks). At the end of the study the intervention group showed improvement in glycosylated hemoglobin and certain inflammatory markers compared to the control group.[76]

In general, in recent years several clinical studies and meta-analyses of studies support the beneficial effects of the consumption of yoghurt enriched with probiotics on the glycemic control of DMII patients.[79,80] In addition, several meta-analyses of studies support that the consumption of probiotics by patients with DMII probably affects, to a moderate degree, the metabolism of glucose, particularly in ≥8 week interventions.[79,81–85] However, it is worth noting that most of these meta-analyses have also included studies which examined probiotics as capsule supplements rather than as an enhanced ingredient in yoghurt. In contrast with the encouraging results of clinical trials and older meta-analyses for the possible effect of enrichment of yoghurt with probiotics, a recent meta-analysis of 9 randomized clinical trials (2019) concluded that there is no statistically significant difference in glycemic control indicators between a conventional and an enriched with probiotics product in patients with DMII or obesity.[86] Consequently, more and well-planned RCTs of over 8 weeks are required and, maybe, it would be useful in examining the intestinal microbiome before and after the intervention, so that possible benefits of yoghurt with probiotics to the intestinal microbiota or/and to the glycemic control of DMII patients could be observed.

Yoghurt enriched with linseed

Linseed is a remarkable source of omega-3 fatty acid alpha-linolenic acid, as well as of phytoestrogen lignans. Thanks to its content of valuable nutrients, it has been supported by various studies that it has antioxidant properties against various disorders, such as atherosclerosis and diabetes, and affects the metabolism of lipids and carbohydrates. The main lignin in flaxseed, the diglucoside secoisolariciresinol diglucoside (SDG), most probably has a positive effect on glycemic control and appears to delay the development of diabetes in rats.[87,88] In addition, the fiber content of linseed may be another supporting factor for glycemic control.[89] Actually the consumption of linseed seems to reduce the glucose absorption speed and the need for insulin production.[90] The fibers in linseed, beyond the direct effect on glycemic control, probably also have indirect effects through the reduction of body weight. Specifically, the high fiber content of linseed increases the feeling of satiety, delays gastric emptying and reduces the consumption of foods rich in energy.[91–93] Finally, it is worth mentioning that the phytoestrogens contained in flaxseed seem to be involved in energy metabolism and suspend the activity of many enzymes involved in cell signaling pathways and in mechanisms inside the cell nucleus, such as cell proliferation and differentiation.[94]

Recently, an effort has been made to investigate the effect of linseed on the glycemic control of DMII patients through yoghurt enrichment. More specifically, a randomized double-blind clinical trial was performed in which 57 diabetic patients participated. For a period of 8 weeks 200 g of 2.5% yoghurt with 30 g of linseed was given to the intervention group, while the control group consumed the same quantity of conventional yoghurt for the same period. At the end of the study a significant reduction of glycosylated hemoglobin, triglycerides, total cholesterol, systolic and diastolic blood pressure of the intervention group in comparison with the control group was observed.[95]

Discussion

Yoghurt is a food of high nutritional value, rich in vitamins, minerals and beneficial microbes.[6] Prospective studies support that its systematic consumption can contribute to the prevention of DMII, through various mechanisms that have not been fully elucidated. Several ingredients are involved in these mechanisms, such as calcium, proteins, vitamins and lactic acid bacteria. Some of these ingredients increase satiety, reducing energy intake, or act directly on the secretory function of the pancreas and reduce insulin resistance. Yoghurt is a low GI food since lactose is the available carbohydrate. However, dairy foods elicit a disproportional increase in insulin response compared to other carbohydrate foods, this is attributed to their higher protein content. Whether consumed alone or as part of meals, yoghurt elicits a similar or lower response than other foods.[96] To date, most of the studies have focused on the effects of yoghurt and in general of dairy products, on the prevention of DMII.[18–21] The RCTs that have been conducted to study the role of these foods in the management of DMII are minimal. Actually, clinical trials concerning the effect of yoghurt on diabetic patients are much fewer and focus on its enrichment with vitamin D, calcium and probiotics, while studies concerning the enrichment with other ingredients are scarce, such as B vitamins and linseed on which there is only one study. The majority of these studies have been conducted in the Asian population. It is therefore desirable to conduct similar studies in other populations. To date, however, most studies examining the effects of fortified yoghurt on glycemic control have focused on probiotic fortification.[75–78,80,97] The probiotics that have been used are usually the strains of *L. acidophilus* and *B. lactis* in different proportions, while the duration of the studies on yoghurt enriched with probiotics mainly concerns a short period of 4–12 weeks. Therefore, further future research is needed in order to elucidate the most effective combination and amount of probiotic strains to be fortified as well as longer duration of dietary interventions. The next two ingredients, after probiotics, with which yoghurt has been enriched and promises benefits in glycemic control of diabetics are calcium and vitamin D. Most studies have investigated the enrichment of yoghurt with these two ingredients simultaneously, usually for a short duration of 12–16 weeks.[40,51,53,54] Calcium and vitamin D appear to affect diabetics through a variety of mechanisms and mainly through actions in the secretory function of the pancreas and in the protection of β-pancreatic cells from oxidative damage.[48–50] However, as in the case of probiotics, other clinical trials, with longer durations are required to clarify their possible mechanisms of action and to draw safe conclusions about their effects on glycemic control. In addition to enriching yoghurt with ingredients such as probiotics, calcium, and vitamin D, very recently researchers have turned their attention to enrichment with other ingredients. Flaxseed is a vehicle of valuable nutrients such as phytoestrogens, fiber and omega-3 fatty acids and may have direct and/or indirect effects on glucose management in diabetic patients. At first glance, the results of flaxseed enrichment were positive.[95] One last ingredient that has recently been studied to enrich yoghurt is the B-complex vitamins. As these vitamins contribute to metabolic regulation and it has been observed that many diabetic patients have low levels of these vitamins, it is considered valid to enhance yoghurt with such vitamins aiming to improve their metabolic profile.[66]

The scientific data, so far, are encouraging about the possible beneficial effects of the systematic consumption of yoghurt enriched with vitamin D, calcium or probiotics on the glycemic control of DMII patients. Flaxseed and B-complex vitamins are the two very recently studied ingredients to enrich yoghurt that researchers have focused on.

However, the interventions that have taken place usually concern a small number of individuals, last for a short period of time (<3 months) and include the ingredients to enrich in different quantities. Therefore, in order for the above data to be confirmed and safe conclusions to be drawn, conducting more and better designed studies is required. It is essential that future research is focused on the study of a bigger sample of diabetic individuals, who will receive the functional yoghurt in ideal quantity with ingredient enrichment for a longer period of time, so that the results are clearer and more unambiguous.

Conflicts of interest

The authors declare that there is no conflict of interest.

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