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Review Article

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Management of Diabetes and Nutritional Supplements

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Abstract

Diabetes, in particular type II diabetes mellitus, is among the most common diseases in particular in the western world, but rapidly expanding also in the rest of the world, drug treatment is relegated to a few drugs, while nutritional intervention and physical activity should be considered as the first option, an increasingly used approach, also thanks to a strong marketing push, is the use of nutritional supplements [1, 2]. This work has the aim of analyzing the most used categories, underlining how, at present, there is no supplement capable of treating diabetes, however negative outcomes due to the pathology itself can be managed.

Keywords: Diabetes, Nutritional Supplements, Fiber, Glycemia, Inflammation, Redox State

Introduction

Diabetic societies in the world, for example, the American Diabetes Association (ADA), but also the Italian Society of Diabetology (SID) recommend the management of type II diabetes mellitus, through physical activity, exercise, and drugs, for the first two are given generic indications that are often disregarded or otherwise not operated continuously, relying almost exclusively on drugs [3-5].

Especially in the last 20 years, the supplement industry has experienced continuous growth, reaching a global turnover of around 100 billion dollars, so the search for new fields of application is increasingly in demand, many pharmaceutical companies have also turned their attention to this field, also because, especially in the USA, it is much easier to launch a supplement on the market, compared to the procedure that a drug must follow [6].

A drug also needs a specific therapeutic indication, a supplement can be much more generic, that is, a drug must be specifically addressed "to the treatment of diabetes", for a supplement it can be declared "can regulate blood sugar", the consumer will interpret both products equally. Analyzing current research, although promising, there are no supplements capable of regulating blood sugar in an alternative way to the drugs used in the treatment of diabetes.

In this work we will analyze the most common, reporting the possible mechanism of action and the supporting literature. On the other hand, we will also analyze the supplements that are proposed for the treatment of diabetes but are in fact effective in moderating what are the negative effects of the pathology, specifically inflammation, in particular, due to AGEs and related production of free radicals.

Nutritional Supplement Supposed to Regulate Glycemia

In both conditions of diabetes, i.e. type I and II, subjects are unable to have adequate glycemic regulation, in the case of type I the only treatment is that through the administration of exogenous insulin; in type II diabetes, on the other hand, the pharmacological approach has the objective of indirectly normalizing blood glucose; the supplements used would have the objective of imitating the actions of drugs, limiting their use or, according to some improper claims, even avoiding their use [7]. In fact, despite having a logic and preliminary studies, even valid ones, at the moment there is no strong evidence to support, some of the most commonly used will be analyzed below.

Fibers, one of the nutritional guidelines in diabetes management is to increase the consumption of fruit and vegetables, in fact, this indication has proven to be effective in regulating blood sugar, certainly part of the effect is due to the fiber content, especially the water-soluble ones. So there are also supplements based on vegetal fibers that aim to regulate blood sugar, in fact, the use of fibers has a precise scientific rationale, namely to decrease the glycemic index value of a meal or food [8].

The glycemic index is defined as the ability of a food to change the blood sugar level; food with a high glycemic index will make the blood sugar vary markedly and rapidly (glycemicindex.com), there is obviously an individual variability, but if you can make the blood sugar vary little, obviously less insulin will be needed to manage this increase. Generally, the fibers used are water-soluble, as these carbohydrate polymers form a gel which slows down gastric emptying and/or intestinal absorption, in some cases, they could decrease the total absorption [9, 10].

β-D-glucans, they are non-starch polysaccharides, composed of glucose with glycosidic bonds b 1-4, they are typically contained in cereals, in particular oats and barley, but also mushrooms, algae, and some vegetables or fruits. They have been considered for at least 100 years, how much dietary fiber manages to slow down the absorption of carbohydrates; it seems they have an immunostimulating potential, but as regards the normalizing action on glycemia, on glycated hemoglobin and insulin, there are no studies on human beings that can fully confirm their action [11].

Glucomannan, is a dietary water-soluble fiber, a polysaccharide isolated from the tubers of Amorphophallus konjac, it has the ability to absorb up to 200% of its weight of water, for this feature it is used in the preparation of foods and supplements that can give a greater sense of fullness and consequently less food intake; forming a gel it has an action on the regulation of glycemia, for example, a recent study on rats would seem to confirm this characteristic; studies in men have not provided results that may suggest glucomannan as an agent that can be used exclusively [12-15] .

Psylium, it is a fiber that is part of the mucilage, retains water and tends to gel; it is used to manage constipation and promote intestinal function, like the other water-soluble fibers it has been proposed for the management of blood sugar, although there are interesting studies in glycemic regulation, the effects are not evident even from meta-analyses carried out that recommend its use exclusively for the treatment of diabetes, it can be useful in assisting the management of diabetes and constipation frequently associated [16-18].

Hypoglycemic agents, we decided not to consider studies carried out according to molecular or in vitro docking techniques, as they represent interesting possibilities but not to be applied at the moment, for example, some plant extracts based on fructans and inulin have proved valid in increasing the secretion of GLP-1 and decrease the action of DPP4 (an enzyme that degrades GLP-1), but having been tested only in vitro were not considered [19].

Another series of vegetable derivatives is that of α-amylase inhibitors. By decreasing the action of this enzyme, the rise in blood sugar due to starches can be slowed down, but this is more effective on raw consumed starches, as cooked ones are partially or totally hydrolyzed, fenugreek extract was tested in this regard but without valid results [20, 21].

Chromium, it acts in regulating the action of tyrosine kinase and phosphotyrosine phosphatase, key enzymes in the action of insulin, for this reason it has been proposed as a hypoglycaemic agent. There are various studies on men but the results are often in contrast and do not provide evidence that integration can be beneficial, this could be due to the different forms of chromium, which affect its assimilation, as it is likely that it is only useful in case of deficiency in the diet [22-24].

Nicotinamide, also known as vitamin B6, one of its features is promoting the secretion (not the de novo synthesis) of insulin, it is also used as an adjuvant in hyperlipidaemias, for both actions it needs high doses that cause side effects, albeit not dangerous, such as skin flushes and diffuse itching, vomiting, diarrhea, and jaundice. Therefore, in addition to the need for further checks, effective doses do not guarantee the necessary compliance by the patient [1, 25].

Zinc, it is involved in the synthesis, storage, and secretion of insulin, therefore intra and extracellular levels are decisive for correct glycemic regulation, some studies correlate this microelement with type II diabetes. Zinc is frequently deficient in the diet, also, due to frequent urination and a partial acid/base imbalance, characteristic of diabetes, it is eliminated to a greater extent, therefore a supplementation would be useful to restore the correct levels and effective in supporting insulin synthesis and secretion, but does not appear to be, in itself, a hypoglycaemic treatment [26, 27].

Cinnamon, it is a spice, now very widespread in the world, also typical of some traditional medicines; various works report a hypoglycaemic effect, even if a unanimous mechanism has not been proposed, it could increase the phosphorylation of the insulin receptor tyrosine kinase, improve the functionality of GLUT4 and slow down gastric emptying; the dosages vary from 300 to 6000mg/d, but, although some with encouraging results, these are obtained in combination with the use of drugs, so not ascribable to cinnamon alone, therefore, also thanks to the low cost, it could be recommended as a valid adjuvant but not as a separate treatment [28-30].

Gymnema Sylvestre, it is a plant widespread in various parts of the world, Asia, Africa, and Oceania, characterized by various traditional medicines such as Ayurveda; it is used in the treatment of diabetes, although the mechanism of action is not well elucidated, given the structural similarity with glucose, it could interfere with the enzymes that metabolize it or with the transporters, it could also have a regenerating effect on β-cells; none of these mechanisms have been confirmed, there are well-established human studies that can confirm their exclusive use for the treatment of diabetes [30-32].

Pycnogenol, it has been used since the Middle Ages for the treatment of diabetes, and in fact, the chemical structure is very similar to metformin, the drug most commonly used in the treatment of diabetes; despite this promising characteristic, there are no human studies that can prove an efficacy comparable to the drug [33-35].

Other plant extracts have been proposed for the treatment of diabetes, but in any case, none of these can boast of studies on a large number and with related follow-ups that can confirm their effectiveness, it should be emphasized that more than one of these (For example Morus, Arctium, Green tea, Aloe), have a valid and proven antioxidant effect, which as will be shown later can be very useful in the management, not of the pathology of diabetes but of the consequences of the pathology itself [1, 30, 36, 37].

Management of Inflammation and Free Radicals

Although promising, as shown above, at present there are no valid reports such as to recommend the use as an alternative to drugs; but as for the fibers and foods that contain them, we can certainly recommend the use of supplements or foods that contain substances with anti-inflammatory or antioxidant properties; one of the worst consequences of the diabetes mellitus and hyperglycemia, in general, is due to the reaction known as glycation, with the consequent production of AGEs and ALEs, molecules with very pronounced inflammatory action, which are certain causes of the typical complications of diabetes (neuropathies, retinopathies, and vascular disease) and consequently ROS production [38-40].

Fish oil, often referred to as omega 3 fatty acids, in fact it should be specified that only eicosapentaenoic acid (EPA) and docosahexaenoic acid (DHA) have this effect, as linolenic acid is also part of this biochemical class, although often included in supplements, does not show the desired effect [41].

Many studies show an anti-inflammatory effect through the regulation of prostaglandin synthesis, in particular through the synthesis of specific mediators such as resolvins [42]. Also specifically for the prevention of complications associated with diabetes and atherosclerosis.

So, therefore, DHA and EPA can be a very useful tool in moderating the damages due to hyperglycaemias and to both type I and type II diabetes, with a dosage of at least 1g per day, which cannot be absolved by diet alone, even if the regular use of fish that contains it is beneficial [41-45].

Polyphenols, is a class of substances with proven antioxidant power, in this sense, there are various studies on humans, although, in more than one case, the antioxidant effect, well-proven in vitro, has not provided the same results, often due to the incorrect standardization of the active principle, but also due to its bioavailability. On the other hand, epigallocatechin gallate, resveratrol, curcumin, quercetin, naringenin, and many others show an important potential, at least in moderating the quantity of ROS, for this reason, the regular consumption of fruits, vegetables, and spices that contain this substance should be strongly recommended, and then eventually to consider the supplements that contain it, always considering them as a support and not a cure. It is interesting to note that some supplements proposed as a curative for diabetes, which has shown conflicting but not entirely negative results, have antioxidant action, for example, alpha-lipoic acid, morus, galega, and arctium, therefore probably their ameliorative effect lies in decreasing the negative effect of ROS, not so much in direct action in regulating blood sugar [46-51].

Conclusion

At the moment, although various classes of substances may be promising, there is no evidence that they can replace drug therapy, even if this is not without side effects; for this reason, a nutritional intervention should be recommended, which includes fiber-rich foods, which possibly also in the form of supplements can regulate blood sugar and antioxidants, such as vitamins and polyphenols, which can significantly mitigate the complications due to diabetes. As regards supplementation, omega3 fatty acids and polyphenols may be useful for managing the negative effects due to glycation, Italian Society for Diabetes produced a statement in this direction [4].

It would be useful to plan accurate studies on some substances that show potential, trying to propose a clear mechanism of action and operating systematically, to clarify if they can be really useful in the treatment of diabetes.

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