

Alpha-amylase inhibition can treat diabetes mellitus

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ABSTRACT

Diabetes mellitus is one amongst the main diseases prevailing worldwide. New therapeutic approaches are being investigated to regulate postprandial glucose levels due to severe side-effects of commercially available anti-diabetic medications. Alpha-amylase is responsible for postprandial glucose levels therefore, different plant extracts with alpha-amylase inhibitory activity are being investigated that might decrease postprandial blood glucose levels, thus being an interesting and novel therapeutic target for diabetes mellitus treatment. A possible strategy to block dietary carbohydrate absorption is to use natural resources as carbohydrate digestive enzyme inhibitors as they have fewer side effects than synthetic drugs. Thus, in this review alpha-amylase inhibitory activity of medicinal plants and their phytochemical compounds are explored that might be helpful within the treatment of diabetes mellitus.

INTRODUCTION

Diabetes mellitus is the most common non infective disease. It had been estimated that 347 million individuals have affected globally in 2011^[1-8] and it will get doubled till 2030. It is a complex disorder caused by increased hepatic glucose production, impaired insulin action and no insulin^[9-15] production, leading to rise in blood glucose level. These abnormalities could lead to other major diseases such as angiopathy, neuropathy, retinopathy, nephropathy^[16]. It is categorised into two types- Type 1 (IDDM) and Type 2 diabetes mellitus and the most prevalent form of this disease is the non-insulin dependent diabetes mellitus (NIDDM 2), related to elevated postprandial hyperglycemia^[17-23].

The alpha-amylases^[24-30] are the calcium metalloenzymes which can't function in the absence of calcium. There are many digestive enzymes in humans and among them the most important one is pancreatic alpha-amylase (EC 3.2.1.1), that act as a catalysis in the reaction which involves the hydrolysis of the alpha-1,4 glycosidic linkages of the starch, amylopectin, amylose, glycogen, and numerous maltodextrins and is responsible for starch digestion. The other important enzyme is alpha-glucosidase or maltase (EC 3.2.1.20) which catalyzes the final step of the digestive process of carbohydrates mainly starch by acting upon 1,4-alpha bonds and producing glucose as the final product^[31]. The large molecules like starch cannot cross the blood brain barrier as glucose has to reach the brain thus; to overcome this problem alpha-amylase cleaves the large starch molecules into smaller fragments of sugars in order to cross the blood brain barrier. If there will be excess conversion of starch to sugars, it will increase the sugar level in blood, then the role of insulin will come into action by ordering cells to metabolize the excess sugar moieties and store as energy sources i. e. glycogen. This cycle is endlessly happening in a healthy person. But in some cases, due to excess activity of amylase enzyme and insulin deficiency or resistance to insulin, level of blood glucose arises which might results in hyperglycaemia. To control hyperglycaemia several studies on inhibition of amylase enzyme activity is being studied. However, if there will be excessive inhibition of pancreatic alpha-amylase, it might cause abnormal bacterial fermentation of undigested carbohydrates in the colon resulting in flatulence and diarrhea^[32].

Three most common anti-diabetic drugs that act mainly by inhibiting carbohydrate digestion and absorption are-

- Acarbose (BAY g 5421) - This inhibitor is of microbial origin and it was the first alpha-glucosidase inhibitor commercially available for diabetes treatment which inhibits the activities of alpha-amylase^[33-39], sucrase and maltase.

- Miglitol- Being a 1-deoxyojirimycin derivative, it strongly inhibits sucrose, glucoamylase and isomaltase activities^[40,41].
- Voglibose- It is of bacterial origin which inhibits the activities of alpha-glucosidase, sucrose, isomaltase and maltase.

Several animals studies have shown that mice treated with acarbose^[42] can slow the breakdown of sucrose and starch^[43], but in comparison with polyphenolic enriched crude natural plant extracts^[44], it is not so effective in reducing blood sugar. Heo and his colleagues isolated diphlorethohydroxycarmalol compound from *Ishige okamurae*, which have alpha-glucosidase and alpha-amylase inhibitory effects over those of acarbose^[45]. Many medicinal plant extracts have high concentrations of tannins, compounds responsible for interfering with gut function and exerting an anti-nutritional effect^[46] and also in reducing the glycaemic response to carbohydrate foods in humans^[47]. In another clinical study, it was shown whether the reduction in blood glucose level was due to reduced food intake in mice which was treated with the *Syzygium cumini* ethanolic extract and tannic acid^[48]. In another study by Oliveira and his colleagues, it had been hypothesized that *P. ramiflora* extract consumption contributes to the reduction of food intake, body weight and the blood sugar. Hence, it was concluded that phenolic compounds present in its extract are effective in reducing weight and decreasing blood sugar and thus associated with the dietary restriction and the inhibition of alpha-amylase^[49-57] activity.

Conventional drugs can treat patient's diabetics by improving insulin sensitivity either by increasing insulin^[58-65] production or decreasing the amount of glucose level in blood and hence regulate blood sugar, however total recovery is yet not possible. Moreover, treatment through conventional drugs doesn't seem to be always satisfactory in maintaining the normal level of blood glucose^[66-71]. Thus, there is urgent requirement of new products for diabetic treatment. Literature survey showed that pharmacologically active components of plants such as vitamins, carotenoids, flavonoids, anthocynins and other phenolic compounds can reduce blood sugar in diabetic patients, inhibit α -amylase^[72-78] (both salivary and pancreatic) and reduces numerous direct and indirect effects of various parameters which might be responsible for the development of diabetes^[79-84]. Over two hundred million people in India have limited access to primary aid centers, so they rely upon traditional system of medicine to cater to their healthcare needs therefore; it will be beneficial to treat diabetes by natural plant extracts^[85].

Conclusion

To control hyperglycaemia, combination of insulin plant leaves and alternative modalities of treatment should be regularly consumed as it will avoid diabetic complications and also fewer the side effects of insulin^[87-94] plant leaves consumption. Novel functional foods having alpha-amylase inhibitory activity could be designed as the alternatives of anti-diabetic drugs with blood glucose lowering property however; they would also cause some side effects.

Therefore, treating diabetes by natural resources appears to be a promising strategy and should be preferred for inhibiting alpha-amylase^[95-99]. There is still more research to be done on the isolation of the principle bioactive compounds of the medicinal plant extracts and more clinical research is essential on the safety use of acute and long- term administration of the natural plant extracts and their phytochemical compounds in type 2 diabetes. Hence, there are two major goals to be accomplished; first one is to collect evidences regarding the response of diabetic patients to the natural pancreatic alpha-amylase inhibitors from preclinical studies and the overall benefits that they are being provided from this treatment. Second one is that more research is required in order to assess properties of individual bioactive compounds like their nature, isolation techniques, purification and analysis techniques that are responsible for the observed effects and also to assess the information about synergistic effects of these bioactive compounds with other metabolites. There should be an aim of establishing effective and safe doses of different anti-diabetic therapies.

This approach is going to be price effective than the currently available commercial drugs, proving to be an important feature since type 2 diabetes mellitus is causing serious health issues in both industrialized and developing countries.

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