

Food-Derived Bioactive Peptides as Functional Ingredients for the Management of Type-2 Diabetes

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Type 2 diabetes mellitus (T2DM) is a chronic metabolic disorder associated with insulin deficiency and/or peripheral insulin resistance. One of the main abnormalities observed in diabetic individuals is the elevated blood glucose concentration particularly in the postprandial state, which in turn plays a pivotal role in pathogenesis development and includes atherosclerosis, retinopathy, nephropathy and neuropathy [1]. Lifestyle changes, such as increasing physical activity and the implementation of a low-sugar diet, is the first line of treatment for T2DM [2]. Furthermore, emerging scientific evidence suggests that certain food components (i.e. food-derived peptides) may have additional beneficial effects for the management of T2DM, due to their ability to act upon and control several of the mechanisms involved in carbohydrate metabolism.

Food-derived peptides are structural components of proteins ranging in size between 2 - 20 amino acids, which are inactive when encrypted in the parental macromolecule. These protein fragments can be generated in different ways and their functionality (bioactivity) is dependent on the length and the amino acids composition present in the sequence [3]. Typically, bioactive peptides must resist degradation during passage through the human alimentary tract and exert their physiological role either in the intestinal tract (local function) or can have a systemic effect after being absorbed at the intestinal epithelium and distributed to the target organ via the blood stream [4]. In addition, bioactivity of the peptide fragments seems to be dependent on selective structural features such as the presence of hydrophobic amino acids in addition to proline, lysine and arginine groups [5].

Bioactive peptides exert their physiological role for the management of T2D through different modes of action. The mechanisms include the regulation of incretin hormones, the release of insulin from pancreatic islets, the inhibition of carbohydrate degrading digestive enzymes and an effect on satiety [6]. A few different peptides of food origin have been identified as potent inhibitors of the enzyme DPP-IV. DPP-IV plays a key role in the inactivation of incretin hormones (i.e. GLP-1 and GIP), which in turn enhance meal-induced insulin secretion and contribute to glucose homeostasis [7]. Furthermore, incretins may play a role in suppressing the release of glucagon, delaying gastric emptying and modulating appetite [8]. Thus inhibition of DPP-IV is crucial for extending the half-life and maintaining the concentrations of active incretins [9]. Quite a considerable number of bioactive peptides of food origin have demonstrated significant inhibitory activity of carbohydrate-degrading enzymes such as α -amylase and α -glucosidase [6]. α -amylase and α -glucosidase inhibitors prevent the breakdown of disaccharides and oligosaccharides into monosaccharides and this results in retarding the absorption of glucose and decreased postprandial hyperglycaemia.

Food-derived bioactive peptides with documented beneficial role in the management of T2DM have been identified in a variety of dietary proteins, with bovine milk proteins being the golden standard [10]. Other sources include soy protein, egg albumin, egg white protein, tuna cooking juice, salmon skin, rice bran, black bean protein, cumin seed protein and others [11,12]. The bioactive peptides are typically released from their parental protein by: a. enzymatic hydrolysis during gastrointestinal digestion (pepsin, trypsin, chymotrypsin etc.), b. microbial fermentation during food production (lactic acid bacteria in fermented dairy products) and c. selective enzymatic hydrolysis using proteases derived from animals, plants or microorganisms (papain, alcalase, thermolysin, pepsin etc.) [13].

The use of bioactive peptides derived from food sources as therapeutic agents for the management of T2DM is promising, yet remains challenging. Although there is scope to use bioactive ingredients from natural sources for replacing synthetic drug inhibitors, the main limitation is reproducibility in relation to bioactivity. The fermentation/hydrolysis process needs to be carefully controlled in order to ensure that bioactive fragments remain intact and at desired levels following product development and furthermore can survive digestion in the human alimentary tract. Furthermore, intervention studies using human or animal models are required to determine bioavailability of bioactive peptides and confirm their efficacy.

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