Mini Review

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Immunomodulatory effects of proteolytic enzymes: meteoric brief review

Abstract

Proteolytic enzymes play crucial roles in digestion and immunomodulatory functions. Proteolytic enzymes commonly found naturally in foods and other naturally occurring supplements like papaya, pineapple, kiwi, ginger etc. Proteolytic enzymes based therapies have proposed these days to treat many immune diseases due to having non-toxic and healthy version of naturopathy immunomodulatory alternatives due to having their unique pathophysiological mechanisms. These immunomodulatory effects are commonly carried out by trypsin enzyme due to the activation of specific T lymphocytes to carry out immunomodulatory effects. Trypsin is reported a normal constituent of the serum with normal concentration of 300mg/1 especially in intestinal origin. Their respective pathophysiological mechanisms of immunomodulation are found to have their role to improve inflammatory responses in renal diseases like interstitial nephritis and glomerulonephritis. These kinds of immunomodulatory effects are found to happen due to the activation and production of expansion of specific T lymphocytes. Serum proteases and serum trypsin are usually bound to the antiprotease, alpha 2 macroglobulin to form complex which is protected from autodigestion and degradation by other serum proteases to retain its own enzymatic activity to carry out immunomodulatory effects.

Keywords: Proteolytic enzymes, serum trypsin, serum proteases, immunomodulatory effects

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Introduction

Proteolytic enzymes are types of enzymes which have inevitable roles in protein digestion, immune function and other vital processes. The three main proteolytic enzymes which produced naturally in your digestive system are pepsin, trypsin and chymotrypsin. Our body also produces these proteolytic enzymes which help into break down of dietary proteins like meat, eggs and fish into smaller fragments called amino acids where they are properly absorbed and digested.[1] Food sources of proteolytic enzymes are Papaya, Pineapple, Kiwifruit, Ginger, Asparagus, Sauerkraut, Kimchi, Yogurt, Kefir. Papayas contain an enzyme called papain that also known as papaya proteinase-I and found in the leaves, roots and fruit of the papaya plant. Papain is also powerful proteolytic enzyme and form ancient times; it has been used as a meat tenderizer due to its ability to break down protein. Pineapples have a powerful proteolytic enzyme called bromelain. Bromelain is also found in the fruit, skin and sweet juice of the pineapple plant and has been used as a natural treatment for a number of ailments in America from very ancient times.[2]

Proteolytic enzymes

Trypsin and chymotrypsin are also derived from pigs and cows called animal-based proteolytic enzymes which can be added to supplement blends, while papain and bromelain come from fruit for non-veg diets. Pancreatic enzyme replacement therapy (PERT) was used in the treatment of pancreatic insufficiency, cystic fibrosis, pancreatic cancer, colorectal cancer and stomach cancer. Trypsin undergoes enteropancreatic recirculation after secreted by the exocrine pancreas and get resorbed from the gut lumen, transported in the blood and again secreted by the pancreas.[3] Because of high molecular weight of trypsin-oc2M complex is limited to the blood stream as macromolecular serum proteins. At sites of inflammations along with increased vascular permeability. Thus trypsin, along with the metabolic serum proteases and antiproteases, complement components and Ig are get delivered at the site of inflammation and therapeutically administered trypsin, when injected or given orally, increases the effective concentration of the protease. It has the immunomodulatory potency to activate the anti-inflammatory response or suppress the proinflammatory response by endorsing its importance in therapy. Indeed, trypsin has a broad cleavage profile and acts as a digestive enzyme in the gut.[4,5]

Mechanism

Immune regulated pathophysiological mechanisms are found to responsible to renal disease, including interstitial nephritis, glomerulonephritis and kidney graft rejection. Renal diseases are primarily mediated by antibodies (SLE, IgA nephropathy) and are critically dependent on T-cell involvement. In previous study, rat allograft arteriosclerosis model was developed, and host's T-cell response is found to direct against an aortic tissue transplant in which the transplant is allogeneic. It is triggered by recognition of the allogeneic histocompatibility antigens followed with alloantigen specific T cells activation and cytokines release. And, T-cell-mediated inflammatory reaction lead to produce cytokines which then activate cells of the reticuloendothelial system and induce a type IV (delayed hypersensitivity type) inflammatory reaction which may manifest multiple sclerosis, type 1 diabetes, rheumatoid arthritis and glomerulonephritis. This similar type of T-cell response can also elicit immunomodulatory effects in chronic kidney graft rejection. Trypsin undergoes enteropancreatic recirculation by owing to active transport up to 10% while oral administered trypsin dose is given to ends up in the blood.[5,6] Interestingly, the three molecules like CD4, CD44, and B7-1 are found to be reported important immunoregulators of the T-cell response and trypsin has a highly selective cleavage profile

on cell surface molecules. In an inflamed tissue, mostly proteins and amino acids have trypsin sites which are masked by glycosylation and embedded within the protein core.[7] In recognition process, the T cells antigen receptors binds to the complex of major histocompatibility molecule and processed peptide fragment excised from the suitable antigen. Upregulation of immunomodulatory components occurs at sites of T-cell-driven inflammation by the release of interferon gamma (IFNy) by T cells at inflamed sites.[6–8] Therefore, cleavage of complexed molecules at sites of inflammation are carried out by trypsin and serum protease along with antiprotease, alpha 2 macroglobulin and could locally maintain the T-cell activation threshold act as physiological regulator of the inflammatory response. Trypsin's therapeutic effects on T-cell-mediated disease may be achieved by eliciting the T-cell-activation threshold at the sites of immune injury kind of more like local immune modulatory effects.[9,10]

Conclusion

Hence, proposed proteolytic enzymes-based therapies could might be considered as next generation safe and cost effective therapeutic tolerogenic delivery to the treat T-cell-dependent immune diseases in humans. But, they may also require the most good initiatives and follow ups their respective evaluations based on its relative immunogenic efficacy based on immunomodulatory effects to carry out the most promising and feasible randomized and controlled therapeutic trials with other conventional immunosuppressive drugs and monoclonal antibodies.

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Conflicts of interest

The author declares that there is no conflict of interest.

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