

nonspecific proteinases (Duckworth et al., 1988). While it is now clear that this hypothesis is incorrect in detail, the initial degradative step occurs in endosomes. The insulin protease makes two or more cleavages in the B chain. This is followed by reduction of the disulfide bonds by GITE, yielding an intact A chain and several B chain fragments. The insulin fragments are then further cleaved probably by multiple proteolytic systems, including lysosomes. A number of careful researches have concluded that lysosomes play little or no role in cellular insulin metabolism.

Insulin protease, also known as insulinase, insulin degrading enzyme (IDE), cleaves the peptide hormone insulin and proceeds through a series of intermediates and that the initial cleavage of insulin is between residues 16 and 17 in the B chain (Duckworth et al., 1979), resulting in a molecule consisting of three peptide chains held together by disulfide bonds.

Most activity of IDE is found in cytosol, small amounts found in other subcellular fractions, including plasma membranes, endosomes, and peroxisomes (Duckworth et al., 1998).

Glutathione-insulin transhydrogenase (GITE) inactivates insulin by splitting the hormone at the disulfide bonds into A and B chains (Varandani, 1972). The enzyme carries out this reaction by catalyzing sulfhydryl-disulfide interchange.

In previous studies about GIT, The locations of GITE were found on four different organs liver (Tomizawa & Varandani, 1965; Tomizawa, 1962) pancreas (Varandani & Tomizawa, 1966), kidney and heart (Varandani, 1972) of three different species (human, bovine and rat). After purification the GITE's have similar physical and enzymatic properties (Varandani & Nafz, 1970).