Enzymes- Activation of zymogens

By

Dr. Bhushan R. Kavimandan
1. Carboxypeptidases:
A carboxypeptidase (EC number 3.4.16 - 3.4.18) is a protease enzyme that hydrolyzes the peptide bond of an amino acid residue at the carboxy-terminal (C-terminal) end.

The first carboxypeptidases studied were those involved in the digestion of food (pancreatic carboxypeptidases A1, A2, and B).

Some, but not all, carboxypeptidases are initially produced in an inactive form; this precursor form is referred to as a procarboxypeptidase.

In the case of pancreatic carboxypeptidase A, the inactive zymogen form - pro-carboxypeptidase A - is converted to its active form - carboxypeptidase A - by the enzyme enteropeptidase.

This mechanism ensures that the cells wherein pro-carboxypeptidase A is produced are not themselves digested. Trypsin also activates procarboxypeptidases proelastase.
2. Chymotrypsin:

**Chymotrypsinogen** is a precursor (zymogen) of the digestive enzyme chymotrypsin. This molecule is inactive and must be cleaved by trypsin, and then by other chymotrypsin molecules, before it can reach its full activity.

Its function is to convert proteins to smaller peptides. This is a very useful safety feature for a protein-digesting enzyme. If chymotrypsinogen were not inactivated in this way, it would digest the pancreas, where it is produced.

Chymotrypsin, a digestive enzyme becomes activated after the proteolysis of the peptide bond between **ARG15** and **ILE16** in chymotrypsinogen by trypsin.

The cleavage of this single bond allows several structural modifications to occur that help form the substrate binding site.

The first step in the activation of the enzyme is the cleavage of the **ARG15-ILE16** peptide bond to form active, π-chymotrypsin. In second step π-chymotrypsin removes Ser14, Arg15, Thr 147 and Asn 148 by the process autolysis and form α-chymotripsin (active form).
3. Trypsin:

Trypsinogen is the precursor form or zymogen of the pancreatic enzyme trypsin. It is found in pancreatic juice, along with amylase, lipase, and chymotrypsinogen.

It is activated by enteropeptidase, which is found in the intestinal mucosa, to form trypsin. Once activated, the trypsin can activate more trypsinogen into trypsin. Trypsin cleaves the peptide bond on the carboxyl side of basic amino acids.

Enteropeptidases removes first 6 amino acids (Val-(Asp)₄-Lys) from C-terminal and convert inactive trypsinogen into active trypsin.
4. Pepsin:
Pepsin is one of three principal proteolytic enzymes in the digestive system. Pepsin is expressed as a pro-form zymogen, **pepsinogen**, whose primary structure has an additional 44 amino acids.

In the stomach, chief cells release pepsinogen.

This zymogen is activated by hydrochloric acid (HCl), which is released from parietal cells in the stomach lining.

Hydrochloric acid creates an acidic environment, which allows pepsinogen to unfold and cleave itself in an autocatalytic fashion, thereby generating pepsin (the active form).

Pepsin cleaves the 44 amino acids from pepsinogen to create more pepsin.