

Proteolytic Enzymes Database

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Abstract

Proteases occur naturally in all organisms. These enzymes are involved in a multitude of physiological reactions from simple digestion of food proteins to regulate a great variety of physiological processes including processing and molecular assembly of nascent polypeptide chain, processing of protein hormone and enzyme precursors to the development and fertilization. Deregulation of proteolytic enzymes leads to human pathologies including arthritis, stroke, dementia, etc. Four mechanistic classes of enzymes have been identified. They are serine proteinase, cysteine proteinase, aspartic proteinase and metallo-proteinase. There is growing literature on proteolytic enzymes. This paper contains updated bibliography of Proteolytic Enzyme and Physico-chemical properties of Proteolytic Enzyme including, enzyme's class, source, EC, molecular weight, N-terminal, C-terminal, thiols, activators, inhibitors, bond specificity and comments. This database will be of high values for researchers and students working in this area.

Key words: Proteolytic enzymes; Serine proteinase; Cysteine proteinase; Aspartic proteinase; Metallo proteinase

Proteolytic enzymes also referred to as proteases and proteinases, degrade proteins by hydrolyzing the peptide bond, proteases can either break specific peptide bonds called limited proteolysis, or break down a complete polypeptide chain to amino acid residues known as unlimited proteolysis. Earlier proteases were classified according to their molecular size, charge or substrate specificity. A more rational system is now based on a comparison of active site, mechanism of action and three-dimensional structure. Four mechanistic classes are recognized by the International Union of Biochemistry. The best characterized protease family is that of mammalian serine proteinases e.g. pancreatic trypsin, chymotrypsin, and elastase. The important features of their active sites are the catalytic triad of Asp102, His57, and Ser195. The catalytic reaction proceeds via a tetrahedral transition state intermediate during both the acylation and deacylation steps of catalysis. The same type of mechanism underlies the action of all other serine proteinases. The conformation of the pancreatic serine proteinases is essentially the same: two similarly folded domains with two-fold axis of symmetry. The P1 amino acid of primary substrate binding site of enzyme defines the substrate specificity.

The cysteine proteinase family is also well characterized. It includes several mammalian lysosomal cathepsins; the cytosolic calcium activated proteases and plant protease papain. Papain is the best-studied member of the cysteine protease family. The catalytic cysteine 25 acts like serine 195 of chymotrypsin. Catalysis reaction proceeds *via* thiol ester intermediate and is facilitated by the side chains of adjacent histidine 159 and aspartic acid 158. The aspartic proteinase family consists of pepsin, renin and many other proteases. The active site residues of aspartic proteinase are aspartic acids 33 and 213. These aspartic acid residues are in close geometric proximity to each other. In the pH range 2.0-3.0, one of the Asp is ionized and the other is unionized. A potent

inhibitor of aspartic proteinase is pepstatin. The metallo-proteinases family include carboxypeptidase A and B. Their active site comprise of zinc, with its three ligands two glutamic acids and one histidine. Another glutamic acid side chain 270, acts as the nucleophile, directly or with the participation of a water molecule.

The proteolytic enzymes also play regulatory roles in a great variety of physiological processes. These include from the processing and molecular assembly of nascent polypeptide chain, processing of protein hormone and enzyme precursors to the development and fertilization (Neurath, 1957; Neurath, 1975; Davie and Fujikawa, 1975; Muller-Eberhard, 1975; Steiner et al. 1975; Zanefeld et al. 1975; Cabib and Farkas, 1971; Bornstein, 1974). Proteases also play a key role in cellular processes like separation of chromosome during mitosis, cell cycle and apoptosis. They have also been widely used as an analytical reagent for sequencing the protein and in the identification and isolation of domain of the more complex multifunctional proteins. Deregulation of proteolytic enzymes lead to human pathologies including arthritis, stroke, dementia, metabolic disorder, blood coagulation defects and cardiomyopathy. Preparations of proteolytic enzymes have been shown to be useful in cancer therapy, digestion, hardening of arteries, inflammation and many other chronic diseases.

There is a vast literature on proteolytic enzymes. Therefore, in the present study an attempt has been made in constructing database containing bibliographical information and physico-chemical properties of proteolytic enzymes.

Construction and Contents of Database

Proteolytic enzymes database was developed using Microsoft Access. The web based interface with the aim of helping users to search for specific information. This user interface has been built

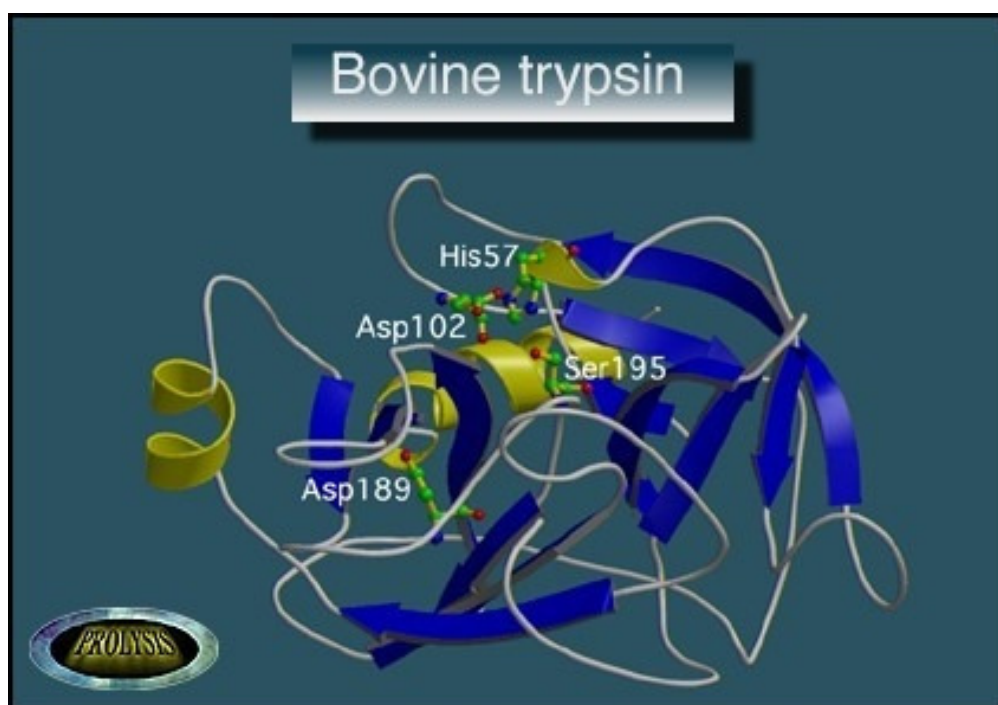
with ASP Server Side Scripts on an Microsoft Windows-based Web Server. Figure 1 shows first page of Proteolytic Enzymes Database. The database can be regularly updated. The bibliographic data for the database was collected from Pubmed [http://www.ncbi.nlm.nih.gov/]. The database contains the bibliographic data from 1989 to 2007. The data for physico-chemical properties on proteolytic enzymes were collected from ExPasy Proteomic Server (http://www.expasy.org).

The database can be accessed through web site http://www.proteolyticenzymes.info. There are 5144 records in the database. The database contains bibliographic informations and informations on physico-chemical properties of a total 30 proteolytic enzymes. The database can be searched by Keywords (in which user can type enzyme name) and by simultaneously selecting "Search Type" option. Alternatively, the database can be searched by selecting enzyme (shown in tabulated form) along with by selecting "Search Type". In "Search Type" menu

option, if "Bibliography of Proteolytic Enzyme" is selected then the database will display the following information on enzyme: Enzyme, First Author, Year, Bibliography Type and Bibliography. Similarly, "About Proteolytic Enzyme" is selected then the database will display these information on enzyme: Enzyme, Class, Source, EC, Molecular Weight, N-Terminal, C-Terminal, Thiols, Activators, Inhibitors, Bond Specificity and Comments.

Utility to the Biological Community

Since proteolytic enzymes hydrolyze food proteins and play a regulatory role in a great variety of physiological processes. Therefore, database of proteolytic enzymes has the potential of becoming major hub of resource for the biological community. This database provides bibliography and Information on physico-chemical properties of proteolytic enzymes to the researchers and students working in this area.



All About Enzyme

Proteolytic enzymes also referred to as proteases and proteinases degrade proteins by hydrolyzing the peptide bond of the protein. Much of the current knowledge of protein structure and function has been derived from the studies on these proteases. Investigation of the kinetics, specificity and inhibition together with the detailed knowledge of amino acid sequence and x-ray structure, have led to the identification of the residues of the active site and geometry of the active site of the enzyme. From these studies the mechanism of action of proteolytic enzymes have been derived. Four mechanistic class of the proteolytic enzymes have been identified. These are Serine Proteinase, Cysteine Proteinase, Aspartic Proteinase and Metallo Proteinase. Proteolytic enzymes play regulatory roles in a great variety of physiological processes. These include from the processing and molecular assembly of nascent polypeptide chain, processing of protein hormone and enzyme precursors to development and fertilization. Protease also play a key role in cellular processes like separation of chromosome during mitosis, cell cycle and apoptosis. Proteolytic enzymes also serve as an analytical reagent for sequencing the polypeptide chain, in the identification and isolation of domain of multidomain protein.

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Search Enzyme [by "Keyword"]

Keywords: Search Type Bibliography of Proteolytic Enzyme Search

Please Select Option to Search [by select "Enzyme"]

<input type="checkbox"/> Bromelain	<input type="checkbox"/> Carboxypeptidase A	<input type="checkbox"/> Cathepsin B	<input type="checkbox"/> Cathepsin K	<input type="checkbox"/> MultiCatalytic Proteinase
<input type="checkbox"/> Renin	<input type="checkbox"/> Carboxypeptidase B	<input type="checkbox"/> Cathepsin C	<input type="checkbox"/> Cathepsin L	<input type="checkbox"/> Proteinase K
<input type="checkbox"/> Thrombin	<input type="checkbox"/> Cathepsin Q	<input type="checkbox"/> Cathepsin D	<input type="checkbox"/> Cathepsin M	<input type="checkbox"/> Chymopapain
<input type="checkbox"/> Plasmin	<input type="checkbox"/> Cathepsin R	<input type="checkbox"/> Cathepsin E	<input type="checkbox"/> Cathepsin O	<input type="checkbox"/> Collagenase
<input type="checkbox"/> Trypsin	<input type="checkbox"/> Cathepsin S	<input type="checkbox"/> Cathepsin F	<input type="checkbox"/> Cathepsin P	<input type="checkbox"/> Chymotrypsin
<input type="checkbox"/> Calpain	<input type="checkbox"/> Cathepsin V	<input type="checkbox"/> Cathepsin G	<input type="checkbox"/> Cathepsin Y	<input type="checkbox"/> Elastase
<input type="checkbox"/> Ficin	<input type="checkbox"/> Cathepsin W	<input type="checkbox"/> Cathepsin H	<input type="checkbox"/> Cathepsin J	<input type="checkbox"/> Papain
<input type="checkbox"/> Pepsin	<input type="checkbox"/> Cathepsin Z			

Search Type About Proteolytic Enzyme Search

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Figure 1: Proteolytic Enzymes Database. The figure shows the front page with three-dimensional structure of enzyme trypsin and a brief summary about proteolytic enzymes. Below summary there is search form given as Keywords and Search type. There is also another alternative search option by selecting enzyme from tabulated list of proteolytic enzymes and Search type.

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