FT-185582

Aprotinin

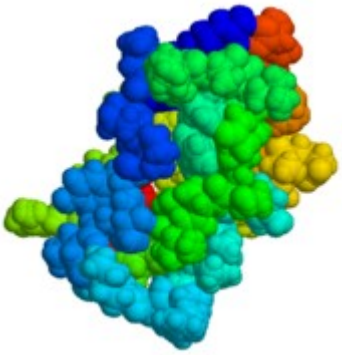
A popular serine proteases inhibitors

Products Description

Name: **Aprotinin** (from Bovine Lung)
Form: powder, lyophilized, approx. 6000 KIU/mg
Syn.Trasylol, Trypsin inhibitor

Catalog number: 185583, 25mg 185584, 100mg
CAS: 9087-70-1
Soluble in water (10 mg/ml, pH = 6 +/- 1)
Activity : 5000 – 7125 KIU/mg
Purity : >95%
Moisture : ≤6%

Formula :
M.W.= 6511.5



Name: **Aprotinin** (from Bovine Lung, PhG)
Catalog number: 24431E, 1g UP24431F, 100g - ~6 Mio.KIU/g
24431A, 50ml – Solution ~200 000 KIU/ml
Form: sterile solution, GMP, PhG

Storage:(L) 4°C (M)
Warm to room temperature before opening
Keep dry (powder).
May be frozen for long term storage.

Competitive, reversible serine protease inhibitor for

- Chymotrypsin,
- Trypsin,
- Kallikrein,
- Plasmin
- factor XII an activator of complement.
- Does not inhibit Factor Xa or thrombin

Scientific and Technical Information

Structure

Aprotinin is a monomeric (single-chain) globular polypeptide derived from bovine lung tissue; it has a molecular weight of 6512 and consists of 16 different amino acids arranged in a chain of 58 amino acid residues, arranged in a single polypeptide chain with three crosslinking disulfide bridges. It was one of the first protein to have its structure solved by NMR, nevertheless, its physiological function was not fully known. Its active center is formed by 4 lysine groups, the tertiary structure shows a pearshaped unit which fits exactly into the binding site of the serine proteinases.

Biolovical Activity

Aprotinin inhibits several serine proteases that forms stable complexes with and blocks the active sites of enzyme. This binding is reversible, and most aprotinin-protease complexes will dissociate at extreme pH levels >10 or <3. Inhibits in particular trypsin, chymotrypsin and plasmin at a concentration of about 125 000 IU/ml, and kallikrein at 300 000 IU/ml[3] . Its action on kallikrein leads to the inhibition of the formation of factor XIIa. As a result, both the intrinsic pathway of coagulation and fibrinolysis are inhibited. Its action on plasmin independently slows fibrinolysis. Because of it's antifibrinolytic activity, it has been used in treatment of myocardiac infarctus, until withdrawn in 2008 as it presents higher risks than aminocaproic and tranexamic acids. It was also initially used in the treatment for acute pancreatitis.

Inhibitory constants:

Enzyme	*activity Ki [M]*
Trypsin, bovine	$6.0\ 10^{-14}$
Trypsinogen, bovine	$1.8\ 10^{-6}$
Chymotrypsin, bovine	$9.0\ 10^{-9}$
Plasmin, human	$2.3\ 10^{-10}$
Kallikrein, pancreatic porcine	$1.0\ 10^{-9}$
Kallikrein, urinary porcine	$1.7\ 10^{-9}$
Kallikrein, urinary human	$9.0\ 10^{-9}$
Kallikrein, plasma porcine	$3.0\ 10^{-8}$
Elastase, leukocytes human	$3.5\ 10^{-6}$
Urokinase, single chain	$2.7\ 10^{-5}$
Urokinase, two chains	$2.5\ 10^{-5}$

Aprotinin is sometimes given in Trypsin Inhibitor Unit (TIU)[]. One TIU will decrease the activity of two trypsin units by 50%, where one trypsin unit will hydrolyze 1.0 µmole of N-alpha-benzoyl-DL-arginine p-nitroanilide (BAPNA) per minute at pH 7.8 and 25°C.

1 TIU = 1 300 KIU.

1TIU = 45 benzoyl-L-arginine ethyl ester (BAEE) µmolar units at pH8.0 at 25°C, or approx. 9 000 BAEE A_{253} units at pH7.6 at 25°C.

Biochemical and Biotechnological Applications

Aprotinin can be used for the isolation of proteins as well as for biopharmaceutical downstream purification to prevent protein degradation during lysis or homogenizaton of cells and tissues: it inhibits undesired proteolytic activity of serine proteases such as trypsin, plasmin, trypsinogen, urokinase, chymotrypsin, kallikrein, elastase and others. It is useful for general purpose and especially for mammalian samples.
It can be used during immunodiffusion, radioimmunoassay or enzyme-linked immuno assay procedures. Standard concentration working range is 0.3 – 0.5µM, but much higher concentrations are used when high enzyme concentration is present such as in cell culture and enzymatic assays.
Aprotinin is also useful in study of antifibrinolytic and pancreatic enzymes. I.e. it is used in chromogenic assays for the determination of antithrombin III, heparin, α2-macroglobulin, factor Xa and thrombin to inhibit disturbing kallikrein or plasmin activities. Small amounts of aprotinin can be added to tubes of drawn blood to enable laboratory measurement of certain rapidly degraded proteins such as glucagon.

Directions for use

Preparation: Freely soluble in water (10 mg/ml) or aqueous buffer solution (e.g., Tris, 0.1 M, pH 8.0).
The aprotinin solution 200 000 KIU/ml is about 33mg/ml
A solution adjusted to pH 7–8 is stable for approximately 1 week at 2-8°C.
Aliquots stored at -15 to -25°C are stable for approximately 6 months.

Working range: 1-100µM (refer to applications above)

Literature

- Shikimi T. *et al*; Japanese journal of pharmacology 1984, vol. 36, no2, pp. 197-203; The enhancing effect of gelatin on aprotinin activity
- Shikimi T.; Japanese journal of pharmacology 1985, vol. 39, no1, pp. 83-89 ; Effects of dextran sulfate on aprotinin activity
- Fritz H, Wunderer G. Biochemistry and applications of aprotinin, the kallikrein-inhibitor from bovine organs. Arzneim Forsch./Drug. Res. 1983; 33: 479-94.

- Lottenberg R, *et al.* Aprotinin inhibits urokinase but not tissue-type plasminogen activator. Thromb Res 1988; 49: 549-56.
- Lemmer JH Jr, *et al.* Aprotinin for coronary bypass operations: efficacy, safety, and influence on early saphenous vein graft patency. A multicenter randomized, double blind, placebo-controlled study. J Thorac Cardiovasc Surg. 1994; 107:543-553
- Sedrakyan A, *et al.* Effect of aprotinin on clinical outcomes in coronary artery bypass graft surgery: A systemic review and meta-analysis of randomized clinical trials. J Thorac Cardiovasc Surg. 2004; 128: 442-448.

Related products:

Other protease inhibitors: i.e. AEBSF UP401071, PMSF #UP147376

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