



pentapharm

Product descriptions

Your partner from lab bench
to finished product





pentapharm

Pentapharm AG

Overview

For its nearly eight decades serving as a global leader in the development and manufacture of advanced biomaterials and superior diagnostic and therapeutic reagents, Pentapharm has earned a reputation as an innovative and reliable supplier of active ingredients for the pharmaceutical and diagnostic industries.

In addition to its broad product scope, Pentapharm offers an exceptional range of specialized customized resources such as peptide synthesis, snake venom enzyme purification, and contract manufacturing services.

In the following pages, we highlight a selection of our biomedical tools and technology. Please feel free to contact us for further information about any of these products, and to learn more about how we can partner with your organization to advance your success in your product development efforts.

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API's and INTERMEDIATES

PENTAPHARM HAS A LONG-STANDING TRADITION as an innovative and reliable supplier of active ingredients for the pharmaceutical and diagnostic industries.

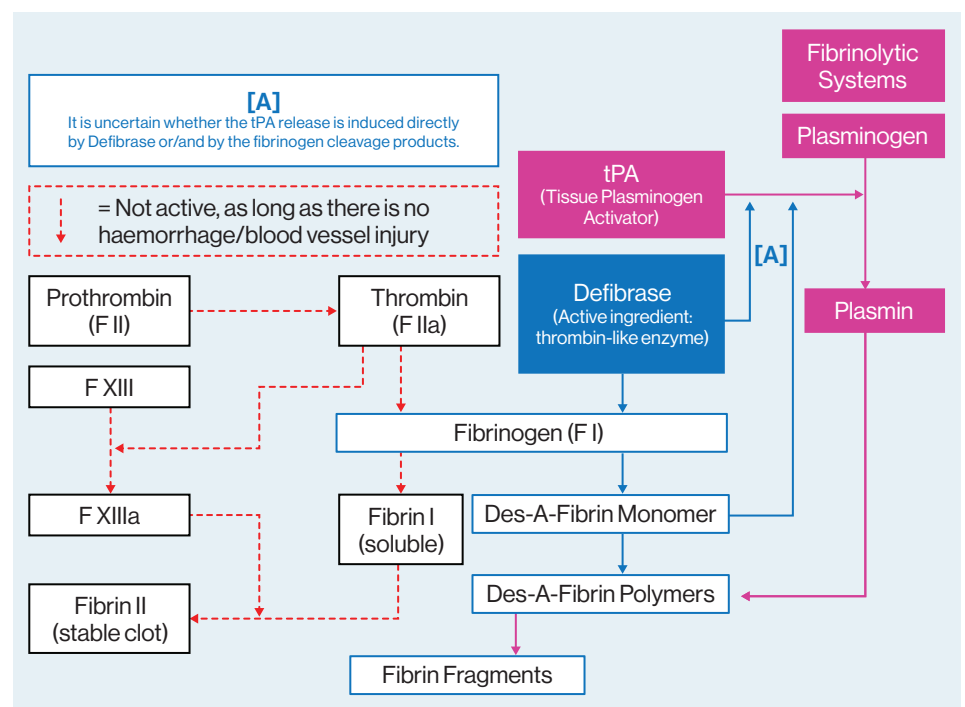
DEFIBRASE®

A thrombin-like proteolytic enzyme isolated from the venom of Bothrops moojeni

A thrombin-like enzyme purified from the snake venom of Bothrops moojeni. Defibrase is a pure single-chain glycopeptide with a molecular weight of approximately 36,000 daltons. In contrast to thrombin, which converts fibrinogen into fibrin by splitting off fibrinopeptides A and B, Defibrase only splits off fibrinopeptide A. The enzyme has a defibrinogenating effect and is used clinically for the treatment of thrombotic diseases.

MODE OF ACTION

- Decreases fibrinogen level and reduces blood viscosity



PHARMACOLOGICAL ACTIVITY

- Decreases fibrinogen levels, anticoagulation, inhibition of thrombogenesis
- Reduces whole blood and plasma viscosity
- Improves hemorheology and microcirculation

APPLICATION

- Acute cerebral infarction
- Ischemia caused by vascular occlusive diseases (e.g., thromboangiitis obliterans, deep vein thrombosis, pulmonary embolism, etc.)
- Peripheral and microcirculatory dysfunctions (e.g., sudden deafness, vibration disease)

HAEMOCOAGULASE

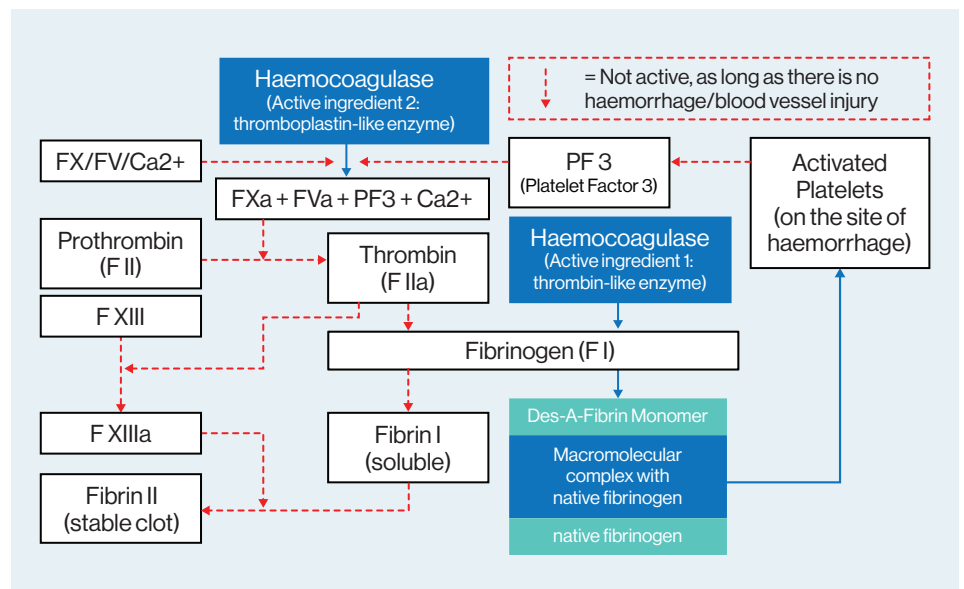
An isolated and purified snake venom enzyme system from *Bothrops atrox*

A haemocoagulant enzyme system free of any toxic protein substances and composed of two different enzymes acting on blood coagulation:

- A thrombin-like serine protease that cleaves fibrinogen to yield Fibrinopeptide A and Fibrin I monomer (Des A-monomer). This enzyme is not inhibited by AT III-heparin complex; inhibited by 2-macroglobulin.
- A thromboplastin-like enzyme which is a metalloprotein leading to activation of FX into FXa, as soon as negatively charged phospholipids become available (at the site of a lesion). FXa converts prothrombin into thrombin which displays multiple actions on platelet aggregation, on activation of plasma factors and on fibrin formation.

MODE OF ACTION

- Enhances the physiological process of blood coagulation



APPLICATION

For many decades, haemocoagulase has been successfully employed for haemostatic applications in the treatment of

- Pulmonary bleeding
- Oral bleeding
- Traumatic bleeding
- Postoperative bleeding
- Other internal and external hemorrhages

PEPTIDE SUBSTRATES

PENTAPHARM HAS DEVELOPED ASSAY METHODS to test for serine protease activity in research, in-process control and quality control. The activity of proteases can be quickly and accurately determined and monitored by use of these peptide substrates.

PEFACHROME®

Used in high throughput screening and quality control of pharmaceutical and other preparations

These substrates are specific synthetic chromogenic peptide substrates for the measurement of the activity of various serine proteases in the areas of coagulation, fibrinolysis, the kallikrein-kinin system, and the complement system. Chromogenic peptide substrates are surrogates that mimic the natural substrate, allowing convenient measurement on an analyzer.

Pentapharm offers substrates for:

Thrombin	Urokinase
Factor Xa	Plasmin
Limulus amebocyte lysate	Trypsin
Activated protein C	C1-esterase
Tissue type plasminogen activator	Factor XIa
Factor IXa	Factor VIIa
Plasma kallikrein	

PEFAFLUOR®

For use in research, in-process and quality control

Fluorogenic substrates are synthetic peptides that react with proteolytic enzymes by releasing a colour that can be followed by spectrophotometry and whose intensity is proportional to the proteolytic activity of the enzyme.

Pentapharm offers substrates for:

Thrombin	Activated protein C
Factor Xa	Tissue-type plasminogen activator
Limulus amebocyte lysate	Factor IXa

ADDITIONAL SUBSTRATES

Amperogenic substrates, custom substrate synthesis and assay development are also available.

INHIBITORS

PENTAPHARM OFFERS A RANGE OF PROTEASE INHIBITORS. They serve to protect specific proteins from proteolytic degradation or to remove undesired proteolytic activity and subsequently increase specificity of proteases or of chromogenic substrate assays.

APROTININ

A polyvalent reversible inhibitor of serine proteases

A single chain polypeptide of 58 amino-acid residues having a molecular weight of 6512, aprotinin is a broad-spectrum serine protease inhibitor of multiple proteolytic enzymes, specifically trypsin- or chymotrypsin-like proteases. It additionally offers anti-inflammatory activities.

Aprotinin inhibits serine proteases with various physiological functions. Important typical proteases inhibited by aprotinin include trypsin, chymotrypsin, kallikreins and plasmin. It additionally weakly inhibits t-PA or u-PA (plasminogen activators), acrosin (essential for conception), human leukocyte elastase (inflammation), and activated protein C (thrombosis).

APPLICATION

Aprotinin can be used to explore a potential contamination of biologicals with serine proteases e.g. kallikrein-like activity in cell culture, plasma fractions, factor concentrates etc. No effect in increasing aprotinin dose = no influence of proteases that are inhibited by aprotinin. Aprotinin can also be employed effectively to make assays more specific, and it protects proteins involved in the assay, e.g. labile coagulation factors or fibrinogen.

Additionally, aprotinin prevents unspecific cleavage of synthetic peptide substrates in chromogenic, amperometric, fluorogenic or luminogenic assays by contaminating proteases or their complexes with 2-macroglobulin. It also protects proteins measure in immunoassays against proteolysis, thus maintaining their integrity.

In cell culture media, aprotinin inhibits degradation of proteohormones, cytokines or other important proteins. It can also extend the life span of certain cells in culture. Finally, injection of aprotinin into lab animals may allow characterization of biochemical pathways which are the subject of proteolysis.

In pharmaceutical areas, aprotinin reduces the risk for perioperative blood loss and the need for blood transfusion in high-risk patients during cardiopulmonary bypass for coronary artery bypass graft surgery. It slows down fibrinolysis, the lysis of blood clots, and protects platelets. It also lends itself for use in Fibrin sealant: Aprotinin is added to fibrin glue to delay the fibrinolytic action of plasmin and to stabilize the fibrinogen (and FXIII) components. Aprotinin preserves platelet function and has anti-inflammatory effects, mediated by inhibition of protease-activated receptors expressed on platelets, vascular endothelium, and neutrophils. Finally, aprotinin prevents entry of virus (e.g. ARS-COV or influenza) into the cell by inhibiting proteolytic steps required.

MODE OF ACTION

As a competitive inhibitor, aprotinin forms a stable non-covalent complex with serine proteases and blocks their active centers in a reversible manner. Binding to serine proteases can be reversed in alkaline (pH 10) and acid environments (pH 5 for most proteases, pH <3 for trypsin and plasmin). At these extreme pH values, it should therefore be possible to separate aprotinin from the protease by chromatography on a molecular-sieve column or by filter dialysis. Aprotinin is only cleaved slowly by most proteases, if at all.

PEFABLOC® SC

An irreversible protease inhibitor with broad specificity for serine proteases

With its superior solubility, stability, inhibitory activity and low toxicity, Pefabloc® SC is suitable for biopharmaceutical downstream purification. It belongs to the family of sulfonyl fluorides which irreversibly block serine proteases. Pefabloc® SC is a potent serine threonine phosphatase inhibitor.

APPLICATION

Pefabloc® SC is used to inhibit the detrimental effects of proteases during preparative protein purification. Due to its low toxicity toward eukaryotic cells, it may be applied in the production of recombinant proteins, during fermentation of transformed cells, where proteolytic digestion may decrease the yield of the desired product. It can be used advantageously to completely inactivate protease K during the preparation of chromosomal DNA in agarose plugs.

In contrast to PMSF, Pefabloc® SC is an excellent blocker of thrombin activity in serum or plasma. In these biological fluids, PMSF interacts in a reversible manner with albumin, which reduces its free concentration and leads to a delay in thrombin inactivation. Pefabloc® SC, however, does not react with serum albumin, and exhibits a threefold higher capacity to inactivate thrombin under similar conditions.

Use Pefabloc® SC to inactivate protease K, for example, during pulsed-field gel electrophoresis (PFGE). With this technique, isolating the genomic DNA requires protease K to degrade cellular components, and this highly resilient protease is difficult to inactivate. Pefabloc® SC inhibits protease K, and protects the stability of restriction enzymes used for further DNA analysis.

ADVANTAGES

Because it is water soluble, Pefabloc® SC is easy to use and can be directly added to aqueous buffers. And because it is non-toxic, it can be readily employed where the use of hazardous compounds represents a risk. Finally, because of its high stability, consistent protease inhibition can be achieved even at pH levels above 7.0 and temperatures above +4°C.

PEFABLOC® FG

Inhibitor of fibrin polymerization

Pefabloc® FG binds with a high affinity to fibrinogen, inhibits fibrin polymerization, modifies the mechanical properties of fibrin clots.

APPLICATION

Pefabloc® FG is added to fibrinogen containing reaction mixtures to inhibit disturbing fibrin-related turbidity, gel formation and fibrin deposition in diagnostic and preparative procedures (e. g., measurement of thrombin generation in plasma). Pefabloc® FG is also used to inhibit fibrin formation during purification and processing of clotting factors and other plasma proteins.

BIOCHEMICALS

PENTAPHARM OFFERS SELECTED STANDARDIZED BIOCHEMICAL PRODUCTS for a wide range of biomedical and manufacturing applications. These include research, production, in-process control, quality control, analytical operations, and purification.

PRIONEX®

A porcine collagen peptide fraction that provides multiple advantages

Prionex® is a 10% aqueous solution of a polypeptide fraction of highly purified dermal collagen of porcine origin which has excellent protein stabilizing properties. Prionex® is prepared by partial hydrolysis and is terminally sterilized. It is free from cartilage, bone and plasma components and is therefore a pure form of partially hydrolyzed gelatine type A. Additionally, Prionex® is free from nucleic acids, polysaccharides and lipids as well as any additives.

APPLICATION

Prionex® can be used advantageously to optimize the stability of biological activity; improve conditions for lyophilisation and heat treatment; eliminate the use of bovine-derived materials; prevent denaturation by chaotropic agents or solvents; and to extend the shelf life of enzymes and proteins. Additionally, Prionex® is additive-free and can serve as a high consistency stabilizer.

Prionex® is a proven stabilizer for in-vitro diagnostic (IVD) applications:

- Protein stabilization
- Preservation of biological activity
- Adsorption prevention
- Shelf-life extension
- Lyophilization and heat treatment excipient
- Blocking agent in immunoassays to reduce non-specific binding

Prionex® is now available in lyophilized form: **Prionex® PELLETS**

ADVANTAGES

Prionex® is freely soluble in water, diluted electrolyte solutions, glycerol and DMSO as well as in diluted ethanol and ammonium sulphate solutions below 20% saturation.

It can be used beneficially to:

- Optimize the stability of biological activity
- Improve conditions for lyophilisation and heat treatment
- Avoid denaturation by chaotropic agents or solvents
- Extends shelf life for enzymes and proteins
- High consistency stabilizer
- Non-toxic and non-antigenic

FINISHED IN VITRO REAGENT KITS

PENTAPHARM DEVELOPS AND MANUFACTURES REAGENTS and test systems for coagulation and fibrinolysis.

PEFAKIT® APC-R

Plasma-based
functional assay

Pefakit® APC-R Factor V Leiden is a plasma-based functional assay for the determination of resistance of Factor Va to inactivation by activated protein C (APC) caused by the factor V Leiden mutation. Control plasmas for confirmation of Factor V Leiden mutation (FV:Q) in assays for determination of the functional phenotype for activated protein C resistance caused by the factor V Leiden mutation.

PEFAKIT® REPTILASE® TIME

Plasma based functional assay
to detect deficiency or
abnormalities in fibrinogen

For the investigation of the last phase of blood coagulation. Due to its heparin insensitivity, the Reptilase® Time can detect fibrinogen polymerization disorders even in the presence of heparin. Useful for the detection of dysfibrinogenemia (congenital and acquired forms); detection of elevated levels of FDPs (eg. in sepsis, DIC, thromboembolic diseases, cancer, liver disease); and the detection of fibrinogen deficiency stages but also elevated levels.

PEFAKIT® TAFI

A plasma-based chromogenic
assay for determination of
Thrombin Activatable
Fibrinolysis Inhibitor
(TAFI) activity

Pefakit® TAFI is a fast assay for the quantification of activated TAFI. A synthetic substrate is selectively cleaved by activated TAFI producing a thiol derivative. This thiol derivative reacts with the colorless Ellman's reagent, splitting off the yellow colored 5-mercapto-2-nitro-benzoic acid moiety. The color change measured at a wavelength of 405 nm is directly proportional to the concentration of TAFI activated by thrombin / thrombomodulin.

PEFACLOT® UFH

A powerful and economic kit to
monitor unfractionated heparin
(UFH) in patient plasma samples.

Relies on direct plasma activation at the level of the prothrombinase complex resulting in a fine-tuned analytical output directly proportional to antithrombotic drug content. RVV-V activates FV. In the presence of added phospholipids, defined quantities of FXa and calcium are added and the prothrombinase complex rapidly formed. The prothrombinase complex formation becomes solely dependent on the activity of FXa and thrombin in the sample.

PENTAPHARM: YOUR PARTNER IN COAGULATION AND HEMOSTASIS

APPLYING THE PRINCIPLES OF NATURE AND CREATING VALUE FOR CUSTOMERS BASED ON PRODUCTS OF NATURAL ORIGIN is the inspiration driving our business. For nearly eighty years, Pentapharm has manufactured naturally-derived active pharmaceutical ingredients (API's) for the management of blood coagulation and thrombosis risk. In addition to its API portfolio, Pentapharm also offers hemostasis diagnostic products. Peptide technologies, snake venom enzymes and kit manufacturing capabilities, all in combination with our quality philosophy, allow us to provide safe products and exceptional solutions that make a difference in the market and create value for society.

ACTIVE INGREDIENT EXTRACTION AND PURIFICATION



- Extraction of natural raw materials (animal, plant or biomass) in aqueous and organic solvents
- Operation in 250 – 2500 L scale in aqueous and organic solvents
- Isolation of actives by filtration, decanting, centrifugation, chromatography and distillation, large scale vacuum drying capacity
- Disperser for oil in water emulsions – rotor/stator and laminar mixing
- Filling machine for a wide range of packaging materials and configurations

SNAKE VENOM ENZYMES



- Secure supply of raw venom from own snake farm
- Animal toxin unit for purifying venoms for API and diagnostic products
- Multiple bench scale chromatography skids and filtration units
- Zoning and equipment concept for eliminating cross contamination
- More than seventy-five years of experience in developing snake venom products

PEPTIDE PRODUCTION



- Liquid and solid phase synthesis and scaling up
- Peptide mimetic and derivatized peptide synthesis
- Chromogenic, fluorogenic and amperogenic substrates
- From analytical (25 mg) samples to commercial batches (up to 2 kg)
- Stability testing and product characterization

DIAGNOSTIC INGREDIENTS AND KITS



- Reagent formulation and handling of plasma up to 30 L batch size
- Own production of critical raw materials, e.g. venom enzymes and lipids
- Automated filling lines (incl. glass preparation) in ISO 8 zone
- Freeze drying units for development and up to 40,000 vials per run
- Flexible labelling, confectioning, coding and packing solutions

CUSTOM/OEM MANUFACTURING



- Development and production of customized actives, reagents and kits
- Manufacturing and tailoring of kits based on customer input
- Services related to customizing, registration and adaptation of kits
- Broad range of capabilities resulting from our outstanding technology background
- Development of extraction processes from natural sources

ACTIVE PHARMACEUTICAL INGREDIENTS



- Purification and formulation of API, including aseptic processing
- Development of excipients and auxiliary products for API production
- Operation in compliance with multiple international GMPs
- Production site and quality system approved by multiple FDAs
- Drug Master File for Aprotinin, Defibrase and Hemocoagulase



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