Thrombin

Targets (10) Biointeractions (8)

IDENTIFICATION

Name

Thrombin

Accession Number

DB11300

Type

Biotech

Groups

Approved, Investigational

Biologic Classification

Protein Based Therapies
Blood factors

Description

Also known as coagulation factor II, thrombin is a serine protease that plays a physiological role in regulating hemostasis and maintaining blood coagulation. Once converted from prothrombin, thrombin converts fibrinogen to fibrin, which, in combination with platelets from the blood, forms a clot.

Medical thrombin is a protein substance produced through a conversion reaction in which prothrombin of bovine origin is activated by tissue thromboplastin in the presence of calcium chloride. Thrombin requires no intermediate physiological agent for its action. It clots the fibrinogen of the blood directly. Failure to clot blood occurs in the rare case where the primary clotting defect is the absence of fibrinogen itself.

Bovine thrombin however, is capable of causing fatal severe bleeding or thrombosis [Label]. This thrombosis may result from the development of antibodies against bovine thrombin [Label]. Bleeding may result from the development of antibodies against bovine factor V [Label]. These antibodies may subsequently cross-react with endogenous human factor V and lead to its deficiency [Label]. Patients who are know or suspected to have antibodies to bovine thrombin

as alternatives to using bovine thrombin.

Protein structure

Protein chemical formula

Not Available

Protein average weight

Not Available

Sequences

```
>sp|P00735|THRB_BOVIN Prothrombin OS=Bos taurus OX=9913 GN=F2 PE=1 SV=2
MARVRGPRLPGCLALAALFSLVHSQHVFLAHQQASSLLQRARRANKGFLEEVRKGNLERE
CLEEPCSREEAFEALESLSATDAFWAKYTACESARNPREKLNECLEGNCAEGVGMNYRGN
VSVTRSGIECQLWRSRYPHKPEINSTTHPGADLRENFCRNPDGSITGPWCYTTSPTLRRE
ECSVPVCGQDRVTVEVIPRSGGSTTSQSPLLETCVPDRGREYRGRLAVTTSGSRCLAWSS
EQAKALSKDQDFNPAVPLAENFCRNPDGDEEGAWCYVADQPGDFEYCDLNYCEEPVDGDL
GDRLGEDPDPDAAIEGRTSEDHFQPFFNEKTFGAGEADCGLRPLFEKKQVQDQTEKELFE
SYIEGRIVEGQDAEVGLSPWQVMLFRKSPQELLCGASLISDRWVLTAAHCLLYPPWDKNF
TVDDLLVRIGKHSRTRYERKVEKISMLDKIYIHPRYNWKENLDRDIALLKLKRPIELSDY
IHPVCLPDKQTAAKLLHAGFKGRVTGWGNRRETWTTSVAEVQPSVLQVVNLPLVERPVCK
ASTRIRITDNMFCAGYKPGEGKRGDACEGDSGGPFVMKSPYNNRWYQMGIVSWGEGCDRD
GKYGFYTHVFRLKKWIQKVIDRLGS
```

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Synonyms

coagulation factor II

Thrombin bovine

Thrombin, Topical (Bovine)

Prescription Products

Search

NAME	DOSAGE	STRENGTH	ROUTE	LABELLER	MARKETING START	MARKETING END

5000unit/vial				Co.			
Thrombostat 10000units	Powder	10000 unit	Topical	Pfizer	1954-12-31	2004-07-26	
Thrombostat 1000units	Powder	1000 unit	Topical	Parke Davis Division, Warner Lambert Canada Inc.	1960-12-31	1997-04-25	
Thrombostat 5000units	Powder, for solution	5000 unit	Topical	Pfizer	1951-12-31	2004-07-26	

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Mixture Products

Search

NAME	INGREDIENTS	DOSAGE	ROUTE	LABELLER	MARKETING START	MARKETING END		
Recothrom	Thrombin (5000 IU/5mL)	Kit		Zymo Genetics	2008-01-29	2016-11-30		
Thrombin-jmi	Thrombin (5000 [iU]/5mL)	Kit		Pfizer Laboratories Div Pfizer Inc.	1995-02-24	Not applicable		
Thrombin-jmi	Thrombin (5000 [iU]/5mL)	Kit		Pfizer Laboratories Div Pfizer Inc.	1995-02-24	Not applicable		
Thrombin-jmi	Thrombin (5000 [iU]/5mL)	Kit		Pfizer Laboratories Div Pfizer Inc.	1995-02-24	Not applicable		
Thrombin-jmi	Thrombin (20000 [iU]/20mL)	Kit		Pfizer Laboratories Div Pfizer Inc.	1995-02-24	Not applicable		

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Categories

Amino Acids, Peptides, and Proteins

Biological Factors

Blood and Blood Forming Organs

Endopeptidases

Enzyme Precursors

Enzymes

Enzymes and Coenzymes

Hematologic Agents

Hemostatics

Hydrolases

Local Hemostatics

Peptide Hydrolases

Proteins

Serine Endopeptidases

Serine Proteases

UNII

25ADE2236L

CAS number

Not Available

PHARMACOLOGY

Indication

Bovine thrombin is a topical thrombin indicated to aid hemostasis whenever oozing blood and minor bleeding from capillaries and small venules is accessible and control of bleeding by standard surgical techniques (like suture, ligature, or cautery) is ineffective or impractical [Label]. Additionally, topical bovine thrombin can also be used in combination with an absorbable gelatin sponge, USP [Label].

Associated Conditions

Refractory to surgical techniques Bleeding

Pharmacodynamics

Little has been reported about the systemic pharmacodynamics and pharmacokinetics of bovine thrombin preparations [2], but it is expected that bovine thrombin elicits similar activities as endogenous thrombin. Subsequently, it is believed that bovine thrombin, like endogenous thrombin, functions as a coagulation factor that converts clotting factor XI to XIa, factor VIII to

way of activating protease-activated receptors on the cell membranes of platelets [L1].

Mechanism of action

Bovine thrombin requires no intermediate physiological agent for its action [Label]. It activates platelets and catalyzes the conversion of fibrinogen to fibrin, which are essential steps for clot formation [Label]. Failure to clot blood occurs in the case where the primary clotting defect is the absence of fibrinogen itself [Label]. The speed with which the bovine thrombin clots blood is dependent upon the concentration of both the bovine thrombin and the fibrinogen present [Label].

U	Proteinase-activated receptor 1	
	Not Available	
	Human	
U	Proteinase-activated receptor 4	
	Not Available	
	Human	
A	Coagulation factor XI	
	activator	
	Human	
A	Coagulation factor XIII A chain	
	activator	
	Human	
A	Coagulation factor XIII B chain	
	activator	
	Human	
A	Fibrinogen alpha chain	
	activator	
	Human	
A	Fibrinogen beta chain	
	activator	
	Human	
A	Fibrinogen gamma chain	
	activator	
	Human	
A	Coagulation factor V	

activator

Human

Absorption

Little has been reported about the systemic pharmacokinetics of bovine thrombin preparations [2], but owing to its topical mode of administration, it is expected that any kind of systemic absorption would be minimal.

Volume of distribution

Little has been reported about the systemic pharmacokinetics of bovine thrombin preparations [2], but owing to its topical mode of application, systemic exposure or distribution to other organs and tissues is not expected.

Protein binding

Little has been reported about the systemic pharmacokinetics of bovine thrombin preparations [2]. Protein binding data is subsequently not readily available, although thrombin functions naturally to interact with a very specific set of clotting factors [1].

Metabolism

Although little has been reported about the systemic pharmacokinetics of bovine thrombin preparations [2], such products are expected to be metabolized in the same way as endogenous thrombin is. Endogenous thrombin does not circulate in the blood as a free, active molecule for very long [3]. After performing its function it is rapidly inactivated after formation of complexes with various circulating endogenous plasma inhibitors (like antithrombin III) [3]. This rapid inactivation prevents the active agent from diffusing into the general circulation. The complexes formed are then generally cleared and eliminated by the liver [3].

Route of elimination

Although little has been reported about the systemic pharmacokinetics of bovine thrombin preparations [2], they are expected to act in much the same way as endogenous thrombin does. Natural bodily thrombin is cleared by two primary separate pathways: (1) through rapid formation of thrombin inhibitor complexes, which are recognized by hepatic receptors and degraded, and (2) via direct binding to thrombomodulin on the endothelium, followed by internalization and degradation [3]. Specific thrombin inhibitors include ATIII, alpha-2M and heparin cofactor II [3].

Half life

Unfortunately, little has been reported about the systemic pharmacokinetics of bovine thrombin preparations [2].

Clearance

into the general circulation [2].

Toxicity

With regards to bovine thrombin, no cases of overdose have been reported so far [2]. Bovine thrombin however, is capable of causing fatal severe bleeding or thrombosis [Label]. This thrombosis may result from the development of antibodies against bovine thrombin [Label]. Bleeding may result from the development of antibodies against bovine factor V [Label]. These antibodies may subsequently cross-react with endogenous human factor V and lead to its deficiency [Label]. Patients who are know or suspected to have antibodies to bovine thrombin and/or bovine factor V should not be re-exposed to the product [Label]. Patients who are administered bovine thrombin should be monitored for abnormal coagulation laboratory values, bleeding, or indeed, thrombosis [Label].

LD50 values are available for rat and mouse models where rat subcutaneous LD50 > 40mg/kg, rat IP LD50 > 40mg/kg, and mouse subcutaneous LD50 > 50 mg/kg (in which the greater than symbol indicates that the toxicity endpoint being tested was not achievable at the highest dose used in the test) [MSDS].

Regardless, the most common adverse reactions following administration of bovine thrombin include hypersensitivity, bleeding, anemia, post-operative wound infection, thromboembolic events, hypotension, pyrexia, tachycardia, and/or thrombocytopenia [Label].

Affected organisms

Humans and other mammals

Pathways

Not Available

Pharmacogenomic Effects/ADRs

Not Available

INTERACTIONS

Drug Interactions

Not Available

Food Interactions

Not Available

REFERENCES

[ISBN:0781728452]
3. EMEA European Medicines Agency Withdrawal Assessment Report for Recothrom (thrombin alpha) [Link]

External Links

PubChem Substance

347911181

Wikipedia

Thrombin

ATC Codes

B02BD30 — Thrombin

- B02BD — Blood coagulation factors
- B02B — VITAMIN K AND OTHER HEMOSTATICS
- B02 — ANTIHEMORRHAGICS
- B — BLOOD AND BLOOD FORMING ORGANS

B02BC06 — Thrombin

- B02BC — Local hemostatics
- B02B — VITAMIN K AND OTHER HEMOSTATICS
- B02 — ANTIHEMORRHAGICS
- B — BLOOD AND BLOOD FORMING ORGANS

FDA label

Download (51.2 KB)

MSDS

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CLINICAL TRIALS

Clinical Trials

Search

PHASE	STATUS	PURPOSE	CONDITIONS	COUNT
2, 3	Withdrawn	Treatment	Minor burns	1
3	Completed	Treatment	Maintenance of surgical hemostasis therapy	1
3	Unknown Status	Treatment	Rebleeding From Gastric Varices / Ulcer, on Gastric Varices	1
Not Available	Terminated	Treatment	Nasal Bleeding	1

PHARMACOEONOMICS

Manufacturers

Not Available

Packagers

Not Available

Dosage forms

Search

FORM	ROUTE	STRENGTH
Kit		
Powder	Topical	10000 unit
Powder	Topical	1000 unit
Powder, for solution	Topical	5000 unit

Showing 1 to 4 of 4 entries

Prices

Not Available

Patents

Not Available

PROPERTIES

State

Solid

Experimental Properties

Not Available

TAXONOMY

Description

Not Available

Organic Acids

Class

Carboxylic Acids and Derivatives

Sub Class

Amino Acids, Peptides, and Analogues

Direct Parent

Peptides

Alternative Parents

Not Available

Substituents

Not Available

Molecular Framework

Not Available

External Descriptors

Not Available

TARGETS

1. Proteinase-activated receptor 1

Kind

Protein

Organism

Human

Pharmacological action

Unknown

General Function

Thrombin receptor activity

Gene Name

F2R

Uniprot ID

P25116

Uniprot Name

Proteinase-activated receptor 1

Molecular Weight

47439.83 Da

References

1. Leger AJ, Jacques SL, Badar J, Kaneider NC, Derian CK, Andrade-Gordon P, Covic L, Kuliopulos A: Blocking the protease-activated receptor 1-4 heterodimer in platelet-mediated thrombosis. Circulation. 2006 Mar 7;113(9):1244-54. Epub 2006 Feb 27. [PubMed:16505172]

2. Proteinase-activated receptor 4

Kind

Protein

Organism

Human

Pharmacological action

Unknown

General Function

Receptor for activated thrombin or trypsin coupled to G proteins that stimulate phosphoinositide hydrolysis. May play a role in platelets activation.

Specific Function

G-protein coupled receptor activity

Gene Name

F2RL3

Uniprot ID

Q96RI0

Uniprot Name

Proteinase-activated receptor 4

Molecular Weight

the protease-activated receptor 1-4 heterodimer in platelet-mediated thrombosis. Circulation. 2006 Mar 7;113(9):1244-54. Epub 2006 Feb 27. [PubMed:16505172]

3. Coagulation factor XI

Kind

Protein

Organism

Human

Pharmacological action

Yes

Actions

Activator

General Function

Serine-type endopeptidase activity

Specific Function

Factor XI triggers the middle phase of the intrinsic pathway of blood coagulation by activating factor IX.

Gene Name

F11

Uniprot ID

P03951

Uniprot Name

Coagulation factor XI

Molecular Weight

70108.56 Da

References

1. Crawley JT, Zanardelli S, Chion CK, Lane DA: The central role of thrombin in hemostasis. J Thromb Haemost. 2007 Jul;5 Suppl 1:95-101. doi: 10.1111/j.1538-7836.2007.02500.x. [PubMed:17635715]

4. Coagulation factor XIII A chain

Human

Pharmacological action

Yes

Actions

Activator

General Function

Protein-glutamine gamma-glutamyltransferase activity

Specific Function

Factor XIII is activated by thrombin and calcium ion to a transglutaminase that catalyzes the formation of gamma-glutamyl-epsilon-lysine cross-links between fibrin chains, thus stabilizing the fibr...

Gene Name

F13A1

Uniprot ID

P00488

Uniprot Name

Coagulation factor XIII A chain

Molecular Weight

83266.805 Da

5. Coagulation factor XIII B chain

Kind

Protein

Organism

Human

Pharmacological action

Yes

Actions

Activator

General Function

The B chain of factor XIII is not catalytically active, but is thought to stabilize the A subunits and regulate the rate of transglutaminase formation by thrombin.

F13B

Uniprot ID

P05160

Uniprot Name

Coagulation factor XIII B chain

Molecular Weight

75510.1 Da

References

1. Crawley JT, Zanardelli S, Chion CK, Lane DA: The central role of thrombin in hemostasis. J Thromb Haemost. 2007 Jul;5 Suppl 1:95-101. doi: 10.1111/j.1538-7836.2007.02500.x. [PubMed:17635715]

6. Fibrinogen alpha chain

Kind

Protein

Organism

Human

Pharmacological action

Yes

Actions

Activator

General Function

Structural molecule activity

Specific Function

Cleaved by the protease thrombin to yield monomers which, together with fibrinogen beta (FGB) and fibrinogen gamma (FGG), polymerize to form an insoluble fibrin matrix. Fibrin has a major function ...

Gene Name

FGA

Uniprot ID

P02671

Uniprot Name

7. Fibrinogen beta chain

Kind

Protein

Organism

Human

Pharmacological action

Yes

Actions

Activator

General Function

Structural molecule activity

Specific Function

Cleaved by the protease thrombin to yield monomers which, together with fibrinogen alpha (FGA) and fibrinogen gamma (FGG), polymerize to form an insoluble fibrin matrix. Fibrin has a major function...

Gene Name

FGB

Uniprot ID

P02675

Uniprot Name

Fibrinogen beta chain

Molecular Weight

55927.9 Da

8. Fibrinogen gamma chain

Kind

Protein

Organism

Human

Activator

General Function

Structural molecule activity

Specific Function

Together with fibrinogen alpha (FGA) and fibrinogen beta (FGB), polymerizes to form an insoluble fibrin matrix. Has a major function in hemostasis as one of the primary components of blood clots. I...

Gene Name

FGG

Uniprot ID

P02679

Uniprot Name

Fibrinogen gamma chain

Molecular Weight

51511.29 Da

9. Coagulation factor V

Kind

Protein

Organism

Human

Pharmacological action

Yes

Actions

Activator

General Function

Copper ion binding

Specific Function

Central regulator of hemostasis. It serves as a critical cofactor for the prothrombinase activity of factor Xa that results in the activation of prothrombin to thrombin.

Gene Name

F5

Uniprot ID

Molecular Weight

251701.245 Da

References

1. Crawley JT, Zanardelli S, Chion CK, Lane DA: The central role of thrombin in hemostasis. J Thromb Haemost. 2007 Jul;5 Suppl 1:95-101. doi: 10.1111/j.1538-7836.2007.02500.x. [PubMed:17635715]

10. Coagulation factor VIII

Kind

Protein

Organism

Human

Pharmacological action

Yes

Actions

Activator

General Function

Oxidoreductase activity

Specific Function

Factor VIII, along with calcium and phospholipid, acts as a cofactor for factor IXa when it converts factor X to the activated form, factor Xa.

Gene Name

F8

Uniprot ID

P00451

Uniprot Name

Coagulation factor VIII

Molecular Weight

267007.42 Da

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