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Trauma

Orthopedics

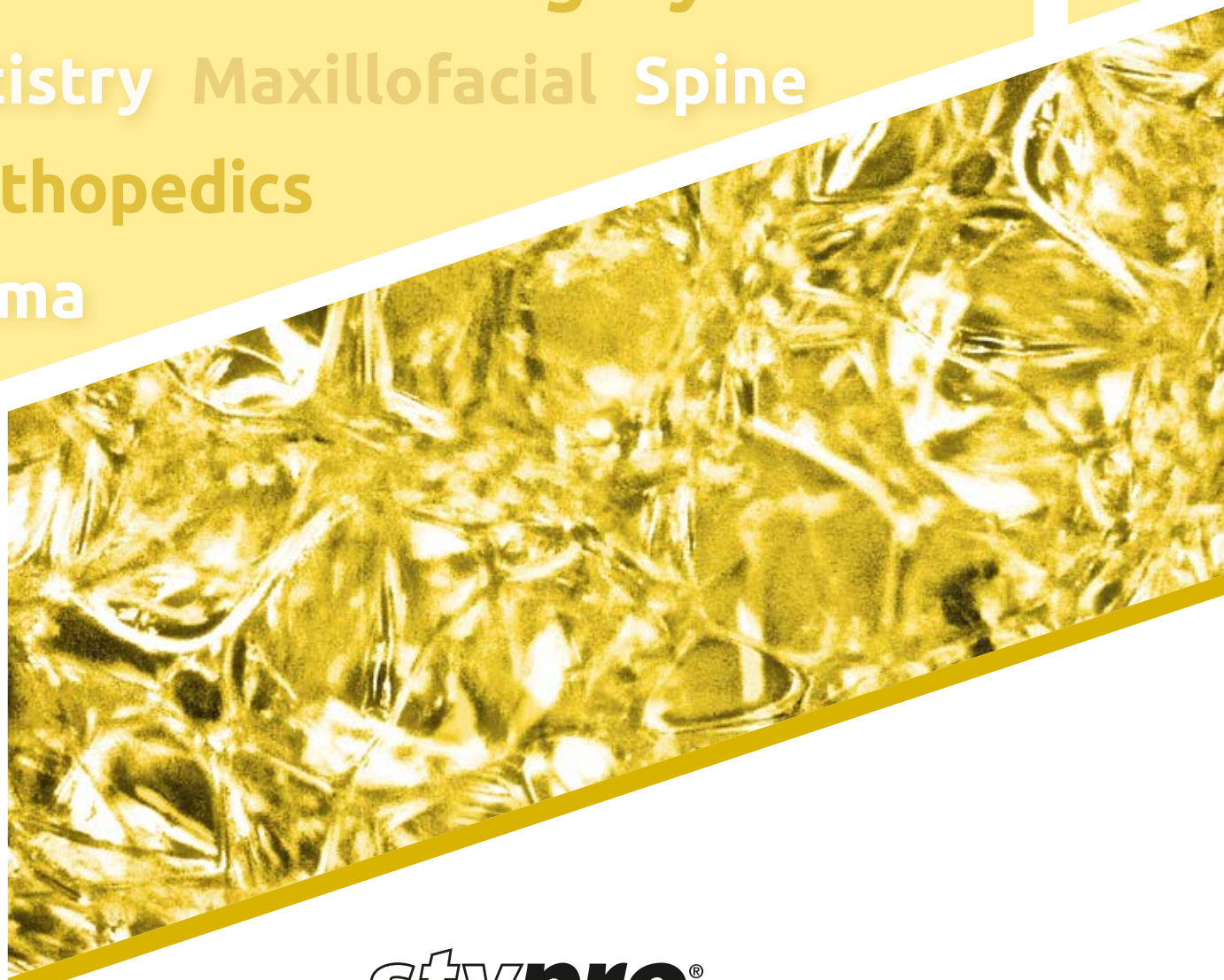
Dentistry **Hemostasis**

Maxillofacial Surgery Trauma

Dentistry Maxillofacial Spine

Orthopedics

Trauma



stypro®

Haemostypticum

Absorbable and implantable gelatine sponge with hemostatic effect

Scientific Information

MADE IN GERMANY
GUARANTEED QUALITY

About curasan

curasan develops, manufactures and markets biomaterials and medical devices in the field of bone and tissue regeneration, wound healing and osteoarthritis therapy. As a pioneer and global technology leader in the growing field of regenerative medicine, curasan is specialized primarily on biomimetic bone grafting materials for dental, oral/maxillofacial, orthopedic and spinal applications, i.e. materials mimicking biological structures.

Numerous patents and a broad record of scientific publications demonstrate the clinical success of curasan's highly innovative products. Clinicians worldwide benefit from the broad range of the premium quality and easy to use portfolio offered by the technology leader curasan. curasan maintains its own high-tech facilities for research, development and manufacturing of biomaterials in Frankfurt/Main, Germany. In addition to its headquarters, the company has a subsidiary, curasan, Inc., in Wake Forest, N.C., USA. curasan's innovative products are cleared by the US Food and Drug Administration (FDA) and many other international authorities and available in almost 50 countries worldwide. curasan AG is a public company listed in the General Standard at the Frankfurt Stock Exchange.

Scientific Information

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1 | Properties

stypro® is a sterile, implantable, porcine gelatine sponge indicated for use in surgical procedures as an adjunct to haemostasis when control of capillary, venous and minor arteriolar bleeding by conventional procedures is ineffective or impractical. The sponge is prepared by foaming a porcine gelatine solution and subsequent drying. The resulting porous structure of **stypro®** has a high capacity to absorb blood corresponding to over 35 times its own weight.

stypro® is an absorbable, topical haemostatic medical device. The gelatine sponge accelerates clot formation by enhancing platelet aggregation. The blood components interact with the enlarged surface of the sponge and the secretions of the wound are soaked through the porous structure. With the adherence of platelets the blood clotting cascade starts. The addition of thrombin is not required to achieve effective haemostasis.

stypro® is completely resorbed within 4 – 6 weeks.

These properties in combination with the excellent tolerance and haemocompatibility of **stypro®** support the tissue repair and natural wound healing. Wound healing is the initial step to tissue regeneration.

Porcine gelatine has no known risk for TSE transmission.

stypro® is a **CE**–certified medical device in accordance with the European Medical Device Directive (93/42/EEC). It is a sterile class III product, which is certified by the mdc as Notified Body (CE 0483).

1.1 Product Characteristics

stypro® is:

- dimensionally stable
- easy to handle
- implantable and completely resorbable
- free from porcine endogenous retroviruses
- useful in tissue repair procedures
- soft and malleable, can be used dry or saturated with sterile physiologic sodium chloride solution
- a sterile gelatine sponge of pure natural origin with excellent biocompatibility.

stypro® has:

- a high capacity to absorb liquids (over 35 times its weight)
- no known risk for TSE transmission
- a rapid haemostatic effect, no exogenous thrombin is needed
- an optimal interconnecting porosity
- an excellent tolerance and biocompatibility

These properties qualify stypro® as an excellent tool for wound management, tissue repair, and natural wound healing.

stypro® provides a safe, effective and comfortable medical device for haemostasis, control of haemocoagulation, wound management, tissue repair and natural wound healing.

Scientific Information

Wound healing process

1.2

The wound healing process is subdivided into three steps:

- **Inflammatory phase**, characterised by platelet aggregation, blood coagulation and invasion of granulocytes, macrophages and leukocytes.
- **Proliferative phase**, characterised by invasion of fibroblasts, angiogenesis, fibroplasia, re-epithelialization and wound contraction.
- **Remodeling phase**, characterised by the production of collagen and matrix proteins to return to the pre-injury phenotype of the tissue.

Moist wound healing has shown to obtain optimal results because most physiologic processes depend on diffusion which cannot take place under dry conditions (Vogt et al). **stypro®**, saturated with sterile physiologic sodium chloride solution can prevent drying of the wound and can be used as a matrix for soft tissue regeneration, comparable to those described by (Ziegler et al).

The gelatine matrix acts as scaffolding, stabilising the blood coagulum. The interconnective porous structure provides a three-dimensional guide-rail for invading blood vessels (angiogenesis) and cells, the prerequisite for tissue regeneration.

2 | Shapes and Sizes

- **stypro® Standard:** 80 x 50 x 10 mm
- **stypro® Cubus:** 10 x 10 x 10 mm
- **stypro® Tampon:** 80 x Ø 30 mm
- **stypro® Special:** 80 x 50 x 1 mm
- **stypro® Special XL:** 125 x 80 x 1 mm
- **stypro® Strip:** 50 x 10 x 10 mm
- **stypro® Sheet:** 80 x 50 x 3 mm
- **stypro® Sheet HP:** 80 x 50 x 3 mm

3 | Application fields

- **stypro® Standard**
  Can be used dry or saturated (with sterile, physiologic sodium chloride solution) in various fields of surgery to stop bleeding, e. g. in wound management (ulcera). **stypro® Standard** can be cut to desired size.

- **stypro® Cubus**
  Is mainly used in oral surgery (dry or saturated) to stop bleeding in extraction sockets or other surgical sites. It may also be used in surgical procedures where the small size of the sponge is an advantage. The Cubus or a piece of Standard can be used to stop bleeding during bone harvesting from the illiac crest by filling the donor site. Use only the amount required to achieve haemostasis and remove any excess.

- **stypro® Tampon**
  Main field of application is rectal surgery, especially haemorrhoidectomy. Subsequent to the surgical procedure the dry **stypro® Tampon** is applied by means of a proctoscope and fixed. The tampon possesses an opening providing the possibility to place a drain. Thus **stypro® Tampon** does not only act as a haemostatic device but also relieves pain. **stypro® Tampon** easily becomes soft, does not adhere to the wound surface and will be excreted spontaneously after 1 – 2 days.

- **stypro® Special**
  Can be used in various fields of surgery, e.g. laparoscopy, spine and neurosurgery, to control intra-operative bleeding. After moistening and rolling, the **stypro® Special** is applied through the trocar. By unrolling the sponge and application, e.g. to the gallbladder bed, the bleeding can be controlled within a short time.

- **stypro® Special XL**
  Currently, it is used for liver surgery and burning surgery or burning wounds.

- **stypro® Strip**
  Main fields of application are oral and maxillofacial surgery and dental surgery after teeth extraction and for filling alveolar defects, or protecting "Schneiderian Membrane" in sinuslift procedures.

- **stypro® Sheet / Sheet HP**
  Is principally used in open surgery as well as in vascular, liver and gall bladder surgery.

4 | Indication fields

stypro® is mainly used for surgical interventions to control capillary, venous, minor arterial and diffuse seeping bleedings in general surgical use, whenever conventional methods are ineffective or impractical.

- Orthopedic, spine and trauma surgery
- Dental surgery
- Plastic and reconstructive surgery
- General and visceral surgery
- Neurosurgery
- Thoracic surgery
- Oncological surgery
- Vascular and cardiovascular surgery
- Ear, nose and throat surgery
- Gynaecological surgery
- Urological surgery
- Haematology
- Dermatology
- Geriatrics
- First aid

Please refer to the instructions for use.

5 | Adverse effects

There are no known adverse effects provided that the product is used correctly in accordance with the instructions for use.
Tissue granulation formation during ENT or middle ear surgery has been reported in at least one animal study (Bahadir et al).

Please refer to the instructions for use.

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6 | Contraindications

stypro® must not be used
- in infected areas
- in case of allergy against proteins of porcine origin
- in conjunction with cemented endoprostheses and when using bone-cement
- in case of osteosynthetic bone surgery between the bone parts
- in case of coagulation disorders, the haemostatic effect may be reduced or eliminated.

Please refer to the instructions for use.

7 | Warnings

Please refer to the instructions for use in this regard.

8 | Technical specifications

Safety 8.1

stypro® is a gelatine-sponge manufactured from porcine collagen (pigskin only). The origin of the pigskin used for the processing of gelatine and the manufacturing of stypro is well controlled and documented. The gelatine corresponds to the quality requirements of the European Pharmacopoeia (EP).

- The cut and ready-packed pieces of **stypro®** are sterilised by Gamma-irradiation.
- With respect to TSE-transmission material of porcine origin is not classified as risk material. The TSE-guidelines of the BfArM (German Drug and Medical Device Agency) are followed during the entire raw material selection.
- The absence of porcine endogenous retrovirus (PERV) in **stypro®** was proven using the Nucleic Acid Amplification Technology (NAT) (Mertsching et al).

Quality requirements of the used pharmaceutical gelatine 8.2

- Controlled origin of the raw material (pig skin).
- The gelatine does not contain, and is not derived from risk material according to the European Decision 2001/2/EC.
- The manufacturing process of the gelatine is certified according to the requirements of DIN EN ISO 13485.
- The processing provides an inactivation of viruses according to EN ISO 22442.
- The gelatine meets the physicochemical and microbiological characteristics conform to the requirements of the European Pharmacopoeia and further requirements according to the internal specification.

8.3 Manufacturing

Raw Gelatine is mixed and dissolved in highly purified water. The mixture is foamed, filled into vessels and dried under controlled conditions. The obtained gelatine sponge is precisely cut into the different shapes and sizes and subsequently double packed, except for the cubus, which is single packed. The ready-packed **stypro®** is finally sterilised by a Gamma-irradiation process.

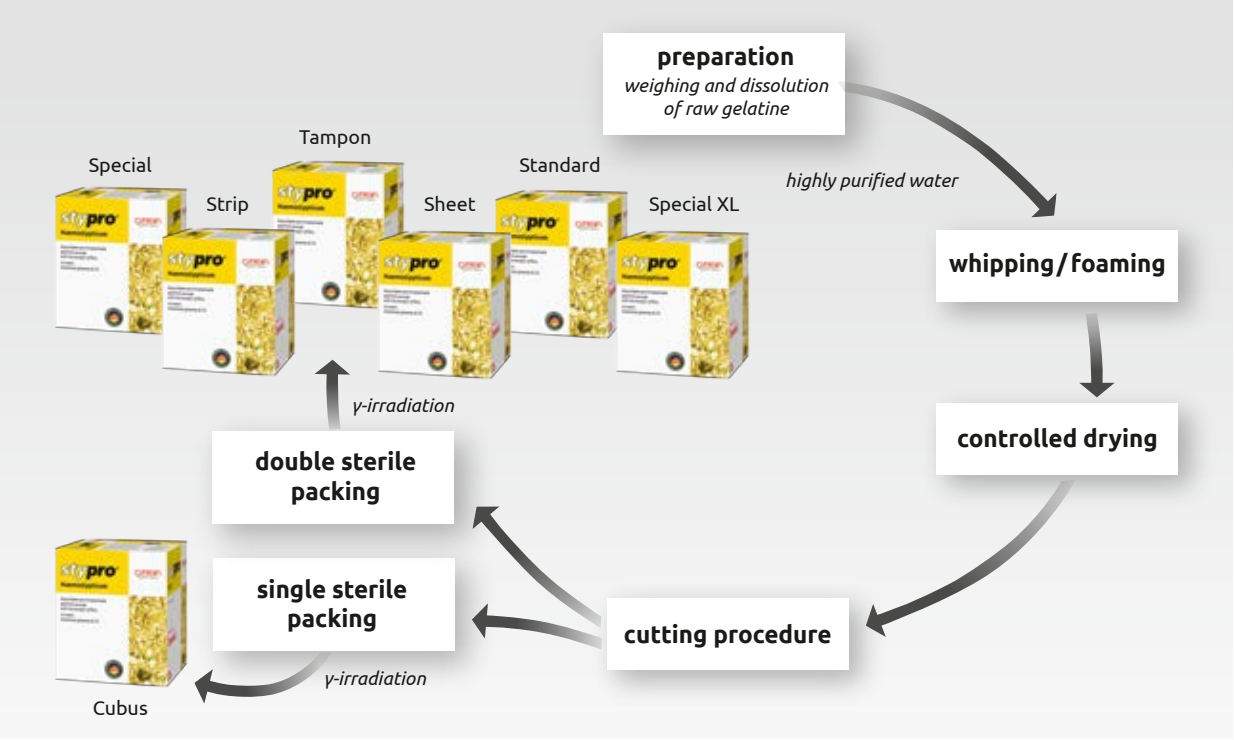

Fig. 2
Manufacturing procedure of **stypro®**

Scientific Information

Specification

8.4

stypro® is a sterile, resorbable gelatine sponge with a haemostatic effect. It is produced exclusively from pharmaceutical gelatine "type A" of porcine origin. The raw material is derived from strictly controlled pig-skin. The suppliers of the raw gelatine granulate are certified companies. The gelatine sponges are obtained from gelatine foam with an interconnective porosity. During the computer controlled drying process the contained water is carefully removed, converting the bubble-structure of the foam into an interconnective three-dimensional structure (see fig. 3). The dried foam is cut into the required shapes, packed and sterilised by Gamma-irradiation.

Due to its high porosity **stypro®** is able to absorb blood over 35 times its own weight. After implantation of appropriate amounts it is completely resorbed within 4 – 6 weeks.

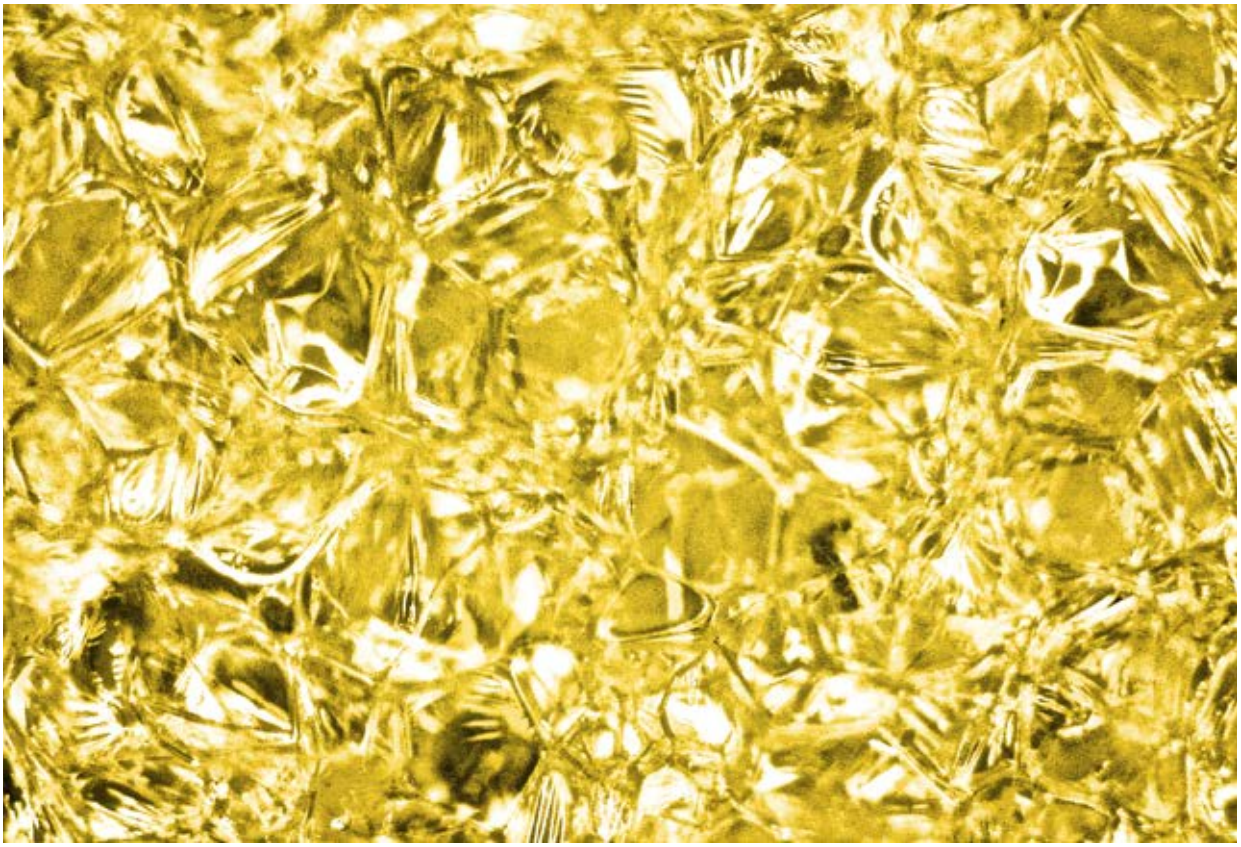

Fig. 3
*The 3D-micro-structure of **stypro®** is obtained through a high-tech manufacturing process.*

8.5 Mode of action

Haemostasis is defined as the whole process of stanching blood whereas coagulation includes only the clotting of plasma with the formation of fibrin. Thus, there is a distinction between primary and secondary haemostasis.

Primary haemostasis concerns the formation of the platelets into a reversible platelet aggregate after a tissue or vessel injury. It is induced by subendothelial collagen structures. However, a clot of thrombocytes alone is not able to form a stable seal of the defect.

Secondary haemostasis concerns the coagulation cascade (see Fig. 4) and – via a series of reactions – forms a stable clot of blood cells and fibrin.

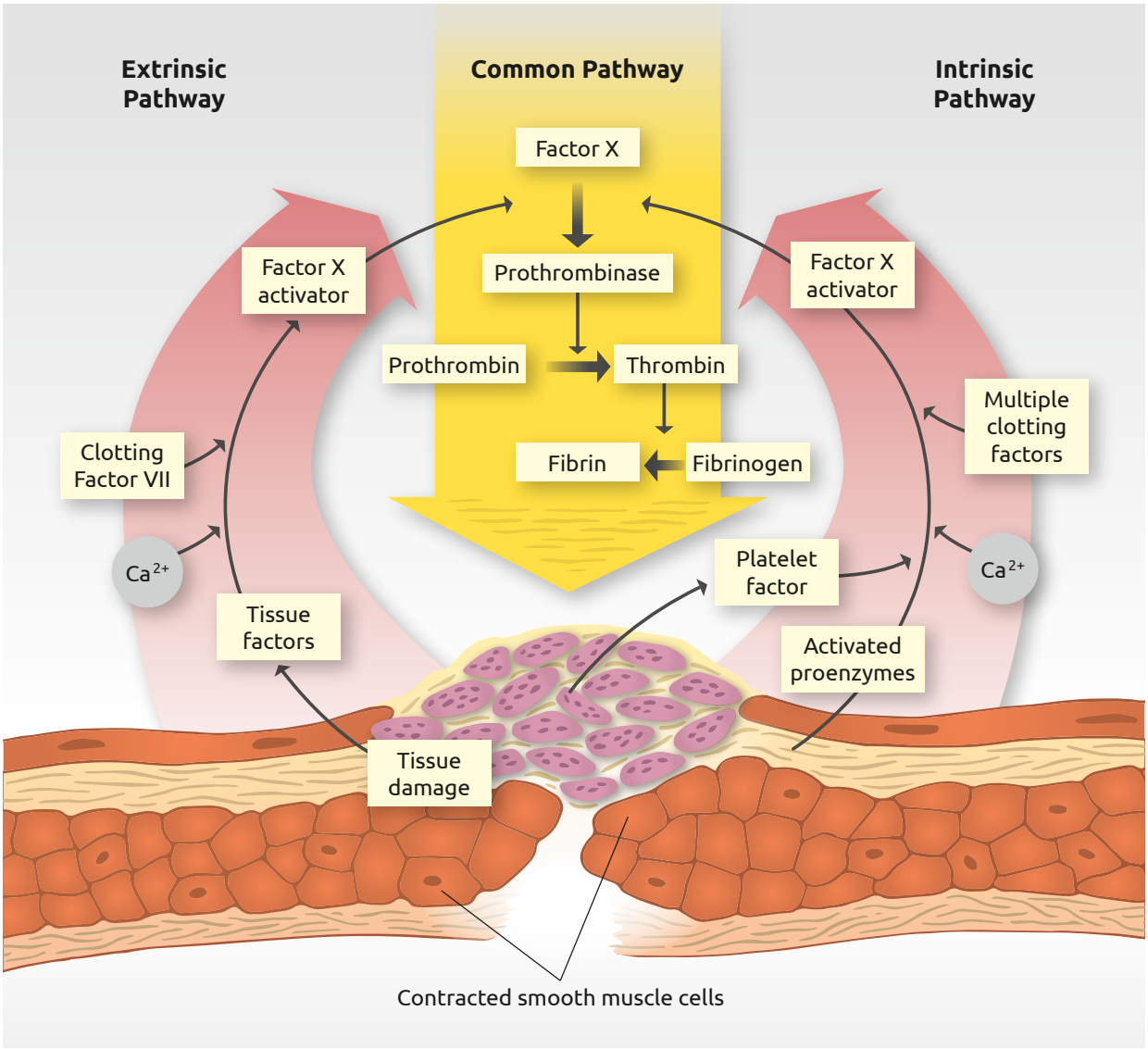

Fig. 4
Intrinsic and extrinsic pathway of blood clotting.

stypro® acts as a topical haemostat. The mechanism of action is not yet elucidated in all details. It is assumed that the haemostatic effect of **stypro®** is rather due to physical properties than due to alterations of the blood clotting mechanism. The gelatine sponge serves as a microfibrillar collagen-like surface activating platelet aggregation in a physiological way. The activated platelets present negatively charged phospholipids (PF3) on their surface and release factor V from their granules. Thus the intrinsic pathway of blood coagulation is started. Factor Va bonds with PF3, forming together with factor Xa in the presence of Ca^{2+}, the prothrombinase complex which converts prothrombin into thrombin.

Another step in the intrinsic pathway activated by the PF3-presenting surface of the platelets is the conversion of factor X into active factor X (Xa), catalysed by PF3-bound factors IXa and VIIIa in the presence of Ca^{2+}.

Besides the conversion of fibrinogen into fibrin, thrombin is a strong agonist for further platelets to be activated. It stimulates chemotaxis of monocytes and has mitogenic effects on lymphocytes, mesenchymal cells, fibroblasts and smooth muscle cells, all involved in tissue regeneration.

After **stypro®** has accomplished its task, it is degraded by specific collagenases followed by unspecific proteases. The released amino acids are either recycled by cells involved in tissue regeneration or partly eliminated.

Caution: stypro® acts as a topical haemostat. In patients taking anticoagulants like phenprocoumon or acetylsalicylic acid the general rules of medicinal and surgical haemostatic procedures have to be obtained.

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