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Pioneering Biomedical Applications with Advanced Macromolecular Conjugate

Introducing

Corline® Heparin Surface Technology CHS™

CHS™ is an advanced, clinically-proven technology that provides biocompatibility for a wide array of medical devices.

The coating uses a unique molecular layering technique: delivering a heparinised surface that overcomes the challenge of minimising thrombotic responses and prolonging device patency in patients.

More than 100,000 patients today have already benefitted from CHS™ modified implants.

CHS™ is a unique non-eluting heparin coating that effectively binds antithrombin, making device surfaces biocompatible.

CHS™ has shown its success in:

- Inhibiting locally-activated clotting on device surfaces
- Reducing platelet and protein adherence and activation
- Minimising coagulation factors, such as FXII

Enhanced Biocompatibility for the New Era of Medical Devices

Dr. Henrik Nittmar,
Chief Executive Officer

"With the device industry rapidly accelerating with new breakthroughs in peripheral vascular intervention, atrial fibrillation, and stroke care among others, the need for a stable, durable, and clinically-trusted biocompatibility coating for both minimally invasive and implantable medical devices has never been higher. I'm excited to bring you Corline Biomedical's unique macro-molecular heparin technology: a coating that has tested exceedingly well across many different devices and truly stands out from anything else available today."

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The Corline® Heparin Surface, CHS™ technology

Immobilised heparin has been used for more than 30 years by the device industry as an excellent bioactive solution for ensuring blood compatibility for medical devices[1]. Over time it has shown its utility in a vast number of clinical applications, and yet, it is the case that heparinised surfaces do not always retain their anticoagulant activity. Corline Biomedical®, however, has solved this essential problem.

Corline Biomedical® has evolved the process and created an improved macromolecular conjugate of heparin, called Corline® Heparin Conjugate (CHC™).

CHC™ uses a single point-attachment of covalently bound heparin to a carrier chain creating effective sites for antithrombin uptake. The CHC™ improves the biocompatibility of both tissue-derived and artificial surfaces by effectively mimicking the only fully blood compatible surface known to man, that of the inner lining of blood vessels.

The Corline Heparin Surface, CHS™, uses the conjugated molecule CHC™ and through a unique bonding process enables it to be applied to any device or surface in one or multiple layers. The proprietary design ensures long-lasting stability and high resistance to chemical challenges and mechanical abrasion.

How CHS™ Stands Out

1. **Provides superior biocompatibility through a unique heparin conjugate layering process which has been shown to effectively increase antithrombin bonding and minimise thrombotic mechanisms:** including inhibition of FXII[2] and reduction in activation of platelets and leukocytes[3].

2. **CHS™ is an extremely durable, stable and flexible coating that:**
   - Bonds firmly to device surfaces with no heparin leakage (non-eluting)
   - Remains stable and effective for long periods, with *in vitro* accelerated fatigue test on CHS™ coated heart valves corresponding to 4.5 years of use[4]
   - Is suitable for all known medical devices that benefit from advanced blood compatibility.

3. **The CHS™ is a versatile coating that can be applied to artificial surfaces and:**
   - Can tailor bioactivity to meet customer and regulatory demands
   - The application technique has no limitations to size of surface area or to medical device material.

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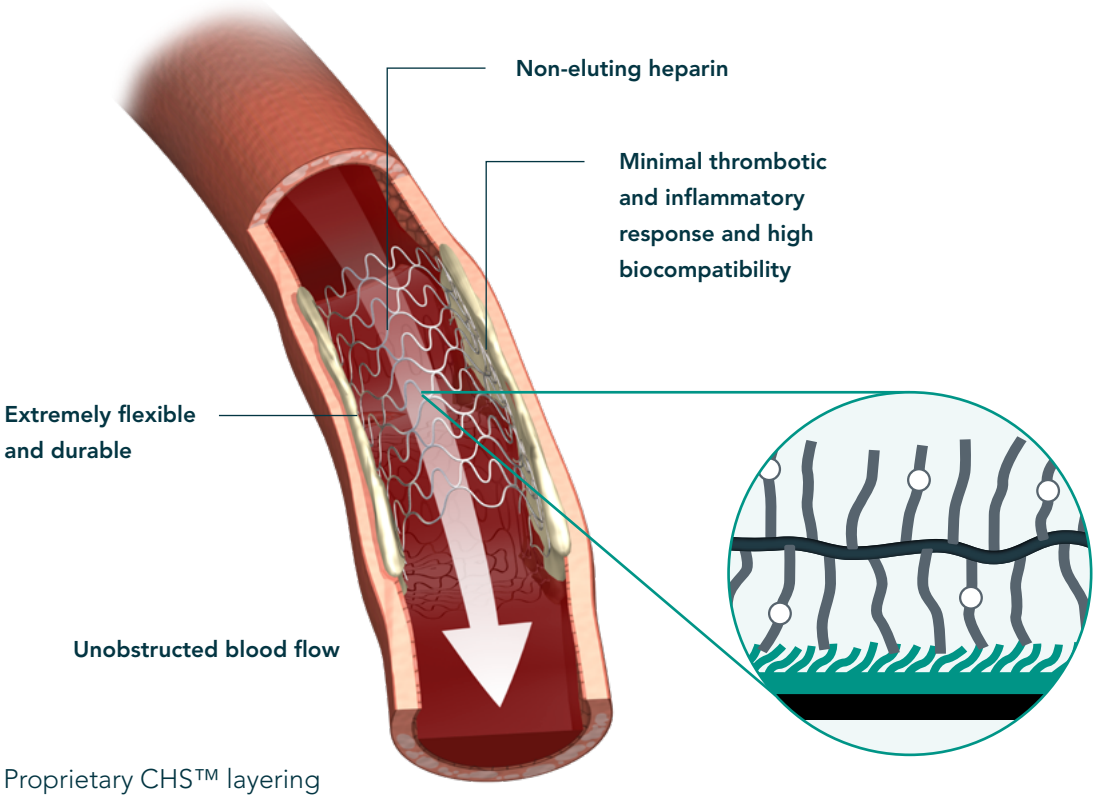
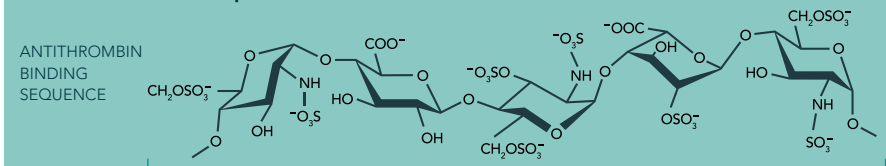
CHS™ Coated Stent in Action

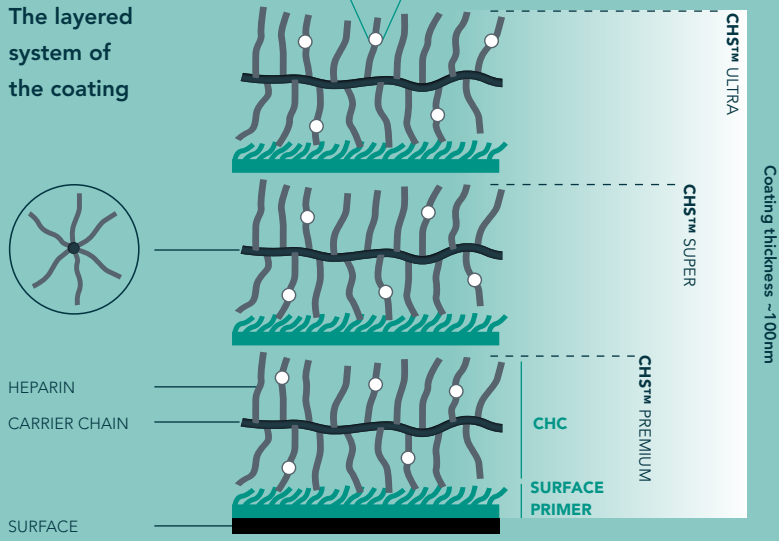


Proprietary CHS™ layering technique presents effective amounts of heparin on the surface, significantly increasing antithrombin uptake, optimising patency, and inhibiting FII, FX and FXII.

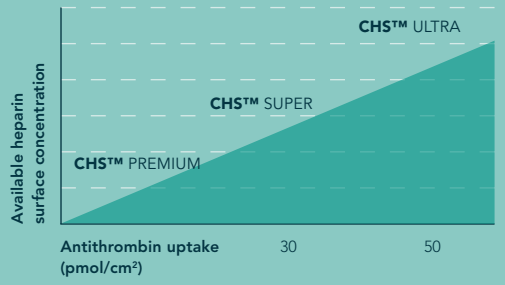
The unique structure of CHS™



The layered system of the coating



Antithrombin binding on par or better than known market solutions



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The Technology Behind CHS™

The CHS™ coating is created by alternating building blocks of primer (modified polyamine) and Corline® Heparin Conjugate (CHC™).

CHC™ is a high molecular weight conjugate with approximately 40-70 unfractionated heparin molecules covalently linked to a carrier chain, a design that results in a high antithrombin binding capacity.

Application of CHS™ to any device or material is done by firstly applying a preconditioning solution to prime the surface and then adding the pre-formed and negatively charged macromolecular heparin conjugate. With additional layers, a sandwich structure is created with interpenetrating network of active binding sites for antithrombin. The CHS™ is extremely thin, measuring approximately 100 nm[5] and the coverage contains only a fraction of the heparin systematically used in routine surgery.

The result is a pioneering and versatile surface coating that modifies any solid surface, artificial or tissue-derived, with the aim of resembling the natural endothelial / glycocalyx blood vessel structure.

Proven Biocompatibility for Any Material or Device

CHS™ coated surfaces have resulted in improved biocompatibility on a wide range of medical devices including cardiovascular stents, extracorporeal circuits for coronary bypass surgeries, dialysis membranes, ablation catheters, microfluidic channels for diagnostic applications, and catheter pumps.

Examples include over 100,000 JOSTENT Plus® coronary stents and 60 Quadrox hollow fibre membrane oxygenators (coating of tubing, cannula, oxygenator and reservoir).

Case Study: Improved Biocompatibility and Biomimicry

CHS™ was a part of a 60 patient clinical trial with coated oxygenator systems. The blood of 45 of the 60 patients was exposed to 9-18 mg CHC™ attached to the 1.8 m^2 oxygenator. No adverse events were seen in patients exposed to the surface and it was seen that leukocyte adhesion to the device was reduced significantly. Five times more granulocytes and almost four times more monocytes were retrieved from the uncoated oxygenator than from the CHS™ ones ($p < 0.001$ and $p = 0.0018$, respectively).[6]

CHS™ Sterilisation and Storage

Our CHS™ technology can be used on materials that need sterilisation post application of the CHS™. The sterilisation can be accomplished by an Ethylene Oxide (EtO) gas process.

The manufacturing technique also gives CHS™ its stability, with a frozen storage time of 56 months for CHC™ and a typical shelf life of 24 months for CHS™ coated devices at ambient temperatures.

Confirmation of Functional Bioactivity

Our CHS™ technology can be applied to a material in a stable sandwich structure. The layer-by-layer structure of CHS™ is also chemically stable and displays high stability towards mechanical or chemical challenges.[7]

The performance of CHS™ in binding antithrombin has been tested thoroughly and the results show that bioactivity increases with more layers used. Plus, platelet adhesion is also reduced, attributed to less fibrinogen deposition produced by the active heparin surface, and the amount of reduction is linked to the increased antithrombin uptake.[8,9] As more CHS™ layers are used, heparin surface concentration increases and the anti-thrombotic mechanism improves.

This we have also seen with our in-house bioactivity protein assay. Here, the CHS™ was exposed to antithrombin and the binding uptake examined with a chromogenic substrate. The result of the bioactivity assays can be seen on page 5: the graph details the amount of anti thrombin on the product surface (pmol/cm^2).

The outcome of both published research and in-house assays are clear:

Corline's unique surface technology delivers improved biocompatibility and offers manufacturers the opportunity to further improve their device patency.

References

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3. Sanchez J. et al. Measuring the degree of plasma contact activation induced by artificial materials. Thromb. Res. 2002, 105:407-412
4. Stasiak JR. et al. Design, development, testing at ISO standards and in vivo feasibility study of a novel polymeric heart valve prosthesis. Biomater Sci 8, 4467–4480 (2020)
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6. Johnell M. et al. Cell adhesion and tissue factor upregulation in oxygenators used during coronary artery bypass grafting are modified by the Corline Heparin Surface. Scandinavian Cardiovascular Journal 2002, 36:351-357
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9. Johnell M, Larsson R, and Siegbahn A. The influence of different heparin concentrations and antithrombin-binding capacity on inflammation and coagulation. Biomaterials 2005 May;26 (14):1731-9

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Manufacturing Options

Corline Biomedical® offer a full service application of CHS™ to your devices:

Full service, in-house application process

Handled by Corline Biomedical's processing and engineering team in Uppsala, Sweden.

Corline Biomedical® is ISO-certified according to ISO 13485:2016 Medical Devices

To support U.S. based product manufacturers, Corline Biomedical® has a Drug Master File (DMF) registered with the U.S. Food and Drug Administration (FDA).

For more information please talk to your official Corline Biomedical® representative.

Corline Biomedical®
CHS Product Sheet: September 2021
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Advanced heparinised coating solutions

Solutions for life.

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