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New Synthetic Antidote of Heparin

One key advantage offered by heparin in cardiovascular surgery relies upon lts high potency and the availability of an antidode allowing its rapid neutralization. Protamine Sulfate (PS) is the only drug available on the market which can counteract quickly and efficiently the action of heparin. Extracted from fishes, PS, a cationic polypeptide, is made from several sub-units with proportion which can change in number and nature. Moreover its natural source represents a potential risk of persistence of residues, such as heavy metals, endotoxins and other antigenic biological contaminants. More recently, due to fishing restrictions in Japan, the availability issue of PS has raised additional issues. Last and not least, moderate to severe side-effects are observed after its i.v. perfusion with a prevalence of about 11 %. To overcome these problems, a research department of University of Liège has developed a synthetic hemocompatible polymer as an alternative to PS for the rapid and efficient neutralization of heparin.

Features

The present invention relates to a novel efficient antidote of heparin (Figure 1). The antidote consists of a synthetic polymer with high affinity and selectivity for heparins (non fractionated and fractionated) in complex biological medium such as human plasma. The polymer can be administered in the form of a liquid wherein the diluent is an isotonic medium or in the form of a lyophilisate wherein the dilutent is a stabiliser.

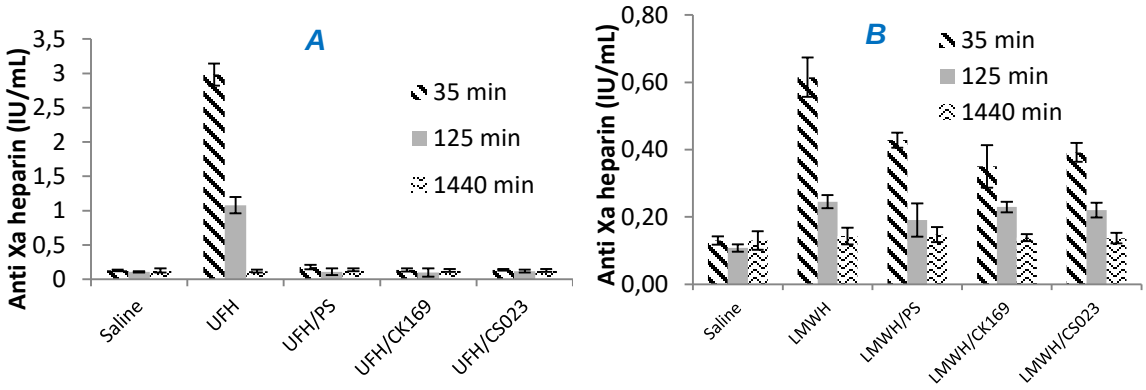

*Figure 1. Percentage of non fractionated heparin (UFH) (**A**) or fractionated heparin (**B**) neutralized either by protamine (PS), either by two synthetic antidotes (CK169 or CS023). Heparins and neutralisation agents have been administrated i.v. on mouse. Neutralisation of the anticoagulants has been verified on blood sampling 35, 125, and 1440 min after polycation injection.*

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Advantages

- In view of promoting interaction with heparin, the new polymer has an extended structure with a flexible polymer backbone that overcomes the problems of other synthetic polymers with more compact structure.
- The range of concentrations to achieve its pharmacological action is identical to PS (i.e. 1 to 2 µg/mL to neutralize the typical doses of heparin used in clinic). This high potency is linked to its specificity, avoiding non-specific interactions with cellular and humoral compounds present in blood.
- Interaction of this polymer with heparin proceeds very quickly (within a time-scale of some minutes).
- Hemocompatible material.
- Easiness to produce on a reproducible way, at an industrial scale and at a very low cost. Its macromolecular characteristics and purity can be easily controlled by macromolecular engineering which allows the adjustment of their composition, length and sequence.

Potential Applications

The new synthetic antidote is intended to be used as a medicament for the treatment of heparin overdose.

Opportunities

The University of Liège is looking for companies interested in research collaboration and/or license agreement.

Patent Status

European Patent Application pending, US Patent granted

Research Team

Prof. Christian GRANDFILS, Director of CEIB, University of Liège
www.ceib.ulg.ac.be ; C.Grandfils@ulg.ac.be

Luca FLEBUS, Master in Biomedical Sciences, PhD student CEIB, ULg

Chantal SEVRIN, Research Assistant, CEIB, ULg

Contact

Gesval S.A.
Mr Eric Feller
e.feller@ulg.ac.be
Tel : +32 4 349 85 28

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