

# Glycosaminoglycans: Anticoagulant and Nonanticoagulant Actions: A Short History of Symposia Held at Villa Vigoni\*

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## Abstract

### Keywords

- glycosaminoglycans
- heparin
- low-molecular-weight heparin
- thromboembolism
- nonanticoagulant effects

Heparin, a sulfated polysaccharide belonging to the family of glycosaminoglycans, was discovered in the beginning of the 20th century and was initially identified as a procoagulant isolated from liver tissue. After the first application in patients approximately 30 years later, further purification identified the major as well as minor, but important, component units of the complex chain mixtures constituting heparin and the multiplex actions became a scientific challenge recently. A series of "Glycosaminoglycan symposium—anticoagulant and nonanticoagulant actions" developed over the past 20 years and focused on this topic has published research data in three issues of *Seminars in Thrombosis & Hemostasis* and in several other international scientific journals. The latest developments on the methods of analysis, the synthesis, the degradation by heparanases and the nonanticoagulant effects in tumor growth, in anti-inflammatory diseases, and in Alzheimer diseases as presented in the 21st symposium are summarized in the present overview on the occasion of the 40th anniversary of the journal with special reference to the journal's founding Editor in Chief, Eberhard F. Mammen.

Heparin was first described by Howell and McLean when they analyzed a thromboplastin substance from the brain and later from liver. Jay McLean was aware of several research results from Germany reporting on peptones from organs acting as thromboplastin.<sup>1</sup> In 1915 and 1916, he purified in the laboratories of W. H. Howell something from the heparophosphate which contaminated the cephalins obtained also from other brain and heart tissues without telling Howell about the results.<sup>2</sup> When Howell became aware of the data his student had published, he went on to analyze the contaminated cephalin and identified them as anticoagulants naming them antithrombin and heparin.<sup>3</sup> Two batches of the purified compound were injected intravenously into dogs

to demonstrate the anticoagulant heparin inhibition of blood coagulation.<sup>4</sup>

The founding Editor in Chief of *Seminars in Thrombosis & Hemostasis*, Eberhard Mammen, contributed to the pathophysiology of blood coagulation and the biological actions of glycosaminoglycans from the mid-20th century.<sup>5</sup> In 1962, he described the benefit of heparin in many indications such as hemodialysis patients.<sup>6</sup> During the period of discovery of low-molecular-weight heparin (LMWH), he investigated their pharmacodynamic effects and speculated about their reduced risk of heparin-induced thrombocytopenia.<sup>7</sup> In a preface to a Glycosaminoglycan Symposium held at Villa Vigoni, he wrote:

The introduction of LMW heparins has opened new avenues for the management of patients with

\* Dedicated on the 40th anniversary of *Seminars in Thrombosis & Hemostasis* to Eberhard F. Mammen, Founding Editor and Editor-in-Chief of this journal until 2008.

# Non Anticoagulant Actions Of Glycosaminoglycans

**Rajendra Varma,Ranbir S. Varma**



## **Non Anticoagulant Actions Of Glycosaminoglycans:**

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