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Polyphosphate in Thrombosis, Hemostasis and Inflammation

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Essentials

- Polyphosphate is present in microorganisms and human cells such as platelets
- Polyphosphate modulates coagulation via interactions with multiple proteins
- Polyphosphate modulates inflammation by triggering bradykinin release and inhibiting complement
- Nucleic acids and polyphosphate co-purify and may be contaminated with silica-based methods

Abstract

This illustrated review focuses on polyphosphate as a potent modulator of the plasma clotting cascade, with possible roles in hemostasis, thrombosis and inflammation. Polyphosphates are highly anionic, linear polymers of inorganic phosphates that are widespread throughout biology. Infectious microorganisms accumulate polyphosphates with widely varying polymer lengths (from a few phosphates to over a thousand phosphates long), while activated human platelets secrete polyphosphate with a very narrow size distribution (about 60-100 phosphates long). Work from our lab and others has shown that long-chain polyphosphate is a potent trigger of clotting via the contact pathway, while polyphosphate of the size secreted by platelets accelerates factor V activation, blocks the anticoagulant activity of tissue factor pathway inhibitor, promotes factor XI activation by thrombin, and makes fibrin fibrils thicker and more resistant to fibrinolysis. Polyphosphate also modulates inflammation by triggering bradykinin release, inhibiting the complement system, and modulating endothelial function. Polyphosphate and nucleic acids have similar physical properties and both will trigger the contact pathway—although polyphosphate is orders of magnitude more procoagulant than either DNA or RNA. Important caveats in these studies include observations that nucleic acids and polyphosphate may co-purify, and that these preparations can be contaminated with highly procoagulant microparticles if silica-based purification methods are employed. Polyphosphate has received attention as a possible therapeutic, with some recent studies exploring the use of polyphosphate in a variety of formulations to control bleeding. Other studies are investigating treatments that block polyphosphate function as novel antithrombotics with the possibility of reduced bleeding side effects.

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Disclosures

SAS and JHM hold patents related to the potential medical uses of polyphosphate and polyphosphate inhibitors. JHM has equity ownership in PrevThro Pharmaceuticals and consults for Cayuga Pharmaceuticals.

Authorship Details

CJB created the graphics; SAS contributed images and wrote the text; CJB, SAS, and JHM contributed to the conceptual design and edited the manuscript.

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