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Effect of His-tag on Biophysical Properties of Selected Staphylokinase Variants

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Thrombosis is a major cause of morbidity and mortality worldwide, emphasizing the need for understanding its mechanisms and treatments. Thrombolytics, fibrinolytic drugs, dissolve blood clots by activating plasminogen to form plasmin, which is then able to break down fibrin. Numerous limitation of presently used thrombolytics justify the importance of their development.

Staphylokinase (SAK), a protein derived from lysogenic strains of Staphylococcus aureus, exhibits potent fibrinolytic activity by forming an equimolar complex with plasmin and selectively activating fibrin-bound plasminogen. This mechanism, coupled with its cost-effective production, positions SAK as a promising thrombolytic candidate.

We analyzed the effect of His-tag on conformational and colloidal stabilities of two naturally occurring forms (SAK STAR and SAK 42D) and their non-immunogenic variants designated as Frida (SAK STAR Frida and SAK 42D Frida). We show that the His-tag has a destabilization effect on all studied SAK variants. In fact, His-variants have decreased thermal transition temperatures and increased rate constants of thermal aggregation. Our analysis indicates that the SAK STAR variants represent, due to their high conformational and colloidal stabilities, perspective candidates for development of an efficient thrombolytic.

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