

The effect of the Ti (IV)-citrate complex on *Staphylococcus aureus* growth and biofilm formation

Gritsenko V., Ajsuvakova O., Tinkov A., Bezryadin S., Gatiatulina E., Ivanova V., Chevela V., Nikonorov A.

Kazan Federal University, 420008, Kremlevskaya 18, Kazan, Russia

Abstract

The primary objective of this study was to investigate the influence of the Ti (IV)-citrate complex on growth dynamics and biofilm formation of *S. aureus*. Speciation analysis was performed in order to estimate the structure of the Ti complex existing in citrate solutions at near-physiological pH. It is estimated that the fully deprotonated tris(citrate) titanate ion $[\text{Ti}(\text{C}_6\text{H}_4\text{O}_7)_3]^{8-}$ predominates in solution at pH 6.46-7.44, and that this is most probably the biologically active form of Ti(IV)-citrate. In in vitro experiments, increasing concentrations of citric acid solutions (0.05, 0.005, 0.0005 M), served as positive controls, while the effects of respective concentrations of Ti(IV)-citrate were examined. The obtained results indicate that citrate decreased *S. aureus* 48 growth at all studied concentrations, whereas *S. aureus* 44 growth was decreased only by high concentrations of citrate (0.05M). Incubation of *S. aureus* culture with Ti(IV)-citrate significantly potentiated citrate-induced effects. Ti(IV)-citrate significantly altered specific bacterial growth rate in a similar manner. The most significant growth reduction was observed at the initial period of bacterial growth. At the same time, the opposite effect was detected in investigations of the effect of citrate and Ti(IV)-citrate on *S. aureus* biofilm formation. Citric acid suppressed *S. aureus* biofilm formation, whereas Ti(IV)-citrate displayed a significant stimulatory effect. Our findings suggest that Ti(IV)-citrate possesses a more pronounced biological effect than citrate. The proposed mechanism of this action is activation of complex transport into the cell and induction of oxidative stress. However, the exact mechanism of Ti(IV)-citrate biological action on bacterial cultures remains unknown.

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Keywords

Bacterial growth, Biofilm formation, Citric acid, *Staphylococcus aureus*, Titanium (Ti)