

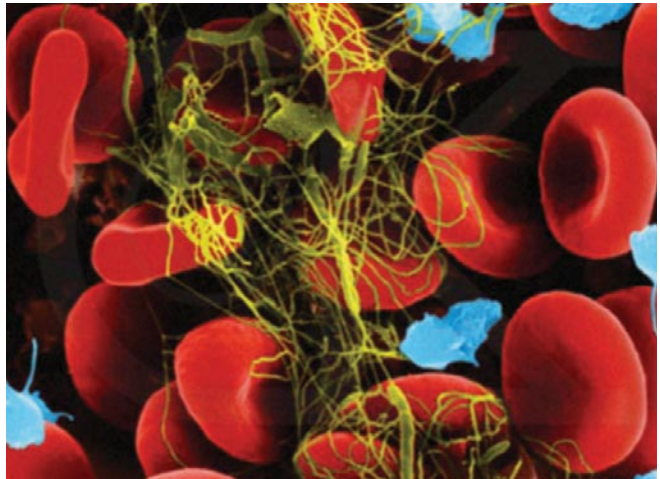
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An investigation into the effects of anti-oxidants on platelet reactivity

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Platelet thrombosis.

Background

Oxidative stress is associated with disturbances in the redox environment of plasma, which potentially affects platelet reactivity, in turn leading to thrombus formation. Although oxidative stress has been shown to play an integral role in the pathogenesis of diseases such as atherosclerosis and diabetes, the role of anti-oxidants in vascular disease prevention is still unclear.^{1,2} Although ascorbic acid (vitamin C) is a known anti-oxidant, there is limited information available regarding the impact of ascorbic acid on platelet function *in vitro*. This investigation is crucial in order to establish mechanisms of action and target sites of anti-oxidants. The focus of this study is to investigate the effects of ascorbic acid on platelet reactivity as indicated by platelet aggregation.

Methods

Platelets were activated using various platelet agonists known to cause platelet aggregation – collagen, thrombin receptor-activating peptide (TRAP), adenosine diphosphate (ADP) and convulxin. Both 'pro-oxidant' and 'anti-oxidant' concentrations of ascorbic acid were used. N-acetyl cysteine (NAC), a known dietary anti-oxidant supplement and pharmaceutical drug, was also tested. The external redox environment of the platelets was altered by combining ratios of both NAC and cysteine (Cys) with cystine (CySS) to form a spectrum of redox couples (NAC/CySS and Cys/CySS) from reducing to oxidising potentials. A platelet aggregometer was used to measure the degree of aggregation.

Results

The data showed that the anti-oxidants ascorbic acid (45µm), NAC (45µm) and cysteine (45µm) inhibited platelet aggregation when platelets were activated with collagen, but not with TRAP or ADP. The reducing NAC/CySS and Cys/CySS redox potentials significantly inhibited platelet aggregation to collagen ($p < 0.0001$), but not to convulxin.

Conclusion

Platelet aggregation is only inhibited when platelets are activated with collagen. Therefore, it appears that the anti-oxidants and redox couples with reducing redox potentials exert a direct effect on the collagen pathway, leading to inhibition of platelet aggregation. We suggest that this is occurring through a modification of integrin $\alpha 2\beta 1$, a collagen-only receptor on the platelet surface. Collagen is a naturally occurring protein in the body, which acts as a potent platelet activator.

Further understanding of the mechanism by which collagen-mediated activation is modulated could aid in the development of novel anti-thrombotic drugs.

Acknowledgements

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References

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