

Can ACE inhibitors inhibit Doxorubicin metabolism?

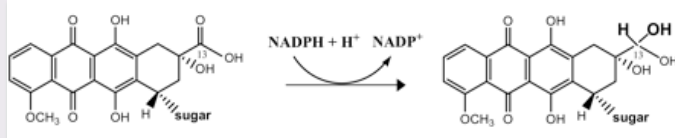
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Aims

To investigate the inhibition of Doxorubicin metabolism by ace inhibitors.



Introduction

- Doxorubicin is a drug used to treat various cancers.
- Doxorubicinol an metabolite of doxorubicin is thought to cause cardiotoxicity.
- Ace inhibitors are proposed to protect against cardiotoxicity, perhaps by inhibition of doxorubicin metabolism.

Methods

- Doxorubicin assay established using human cytosol and idarubicin as internal standard.
- Demonstration of the metabolism of Doxorubicin to Doxorubicinol by incubating with cytosol at varying times.
- Investigation of possible inhibition by various ACE Inhibitors.

Results

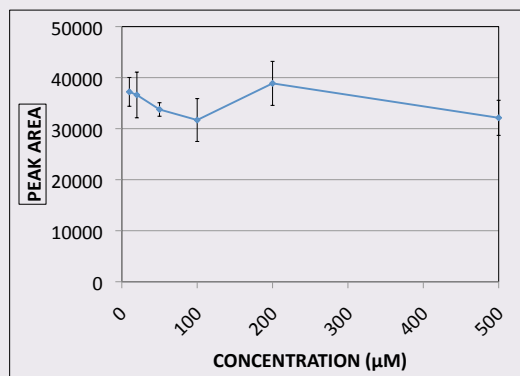


Fig.1. Inhibition of doxorubicin metabolism with perindopril. This graph shows that there was no inhibition of doxorubicin metabolism up to 500µM Perindopril.

Conclusions

At clinically-relevant concentrations (2µM), ACE Inhibitors did not inhibit the metabolism of doxorubicin.

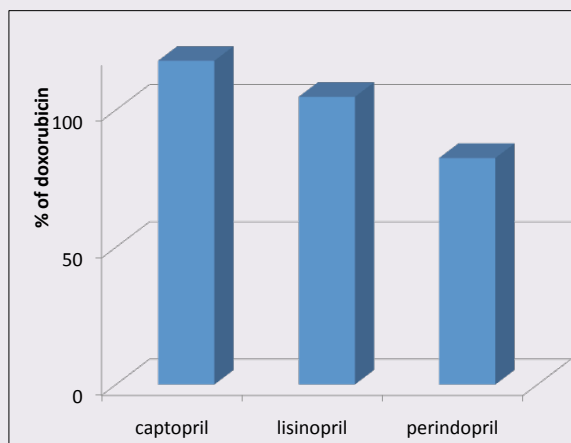


Fig.2. Percentage of doxorubicin compared to no inhibitor. This graph shows that perindopril inhibited doxorubicin metabolism more than lisinopril and captopril. However there was little inhibition overall.

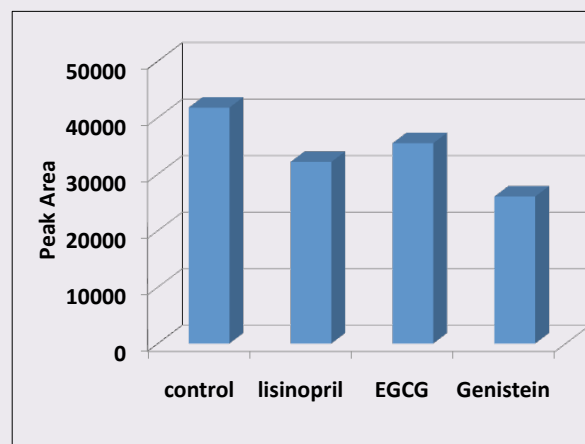


Fig. 3. Compares inhibition of lisinopril to the positive control, EGCG & genistein at 100µM for all 3 inhibitors. This graph shows that 500µM lisinopril inhibited doxorubicin metabolism more than 100µM genistein but less than 100µM EGCG.