

## Cardioprotective and cardiotoxic effects of flavonoid quercetin on rat embryonic heart-derived female H9c2 cells

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Naturally occurring flavonoid quercetin is capable of scavenging free radicals and possess antioxidant properties. Present study explores cardioprotective and cardiotoxic effects of quercetin on rat embryonic H9c2 cardiomyocytes. MTT reduction assay method was used to assess H9c2 cell viability upon quercetin pre-treatment and exposure to hydrogen peroxide (H<sub>2</sub>O<sub>2</sub>). Moreover, various concentrations of quercetin (1-100 µM) were used to determine the toxic effects on H9c2 cells over time (i.e. 24, 48 & 72hrs). Western blotting technique was used to investigate phosphorylation of Extracellular signal Regulated Kinase (ERK) in quercetin exposed H9c2 cells. Morphology of H9c2 cells were studied using coumassie blue staining. H9c2 cells pre-treated (30 min) with quercetin (100 µM and 30 µM) followed by 2hr incubation with 600 µM H<sub>2</sub>O<sub>2</sub> significantly protected the cells from H<sub>2</sub>O<sub>2</sub>-induced cell death. H9c2 cells pre-treated with 100µM quercetin (#p< 0.05 vs H<sub>2</sub>O<sub>2</sub>) were significantly better protected than 30µM quercetin pre-treated cells in H<sub>2</sub>O<sub>2</sub>-induced cell death (\*\*p< 0.01 vs control; n=5). Phosphorylation of ERK increased in the presence of 600µM H<sub>2</sub>O<sub>2</sub> alone. Whereas, quercetin (100 & 30µM) pre-treatment effectively reduced the phosphorylation of ERK (followed by 2hrs 600 µM H<sub>2</sub>O<sub>2</sub> exposure) in H9c2 cells. Total-ERK levels were unaffected in (with/without) quercetin pre-treatment. Morphology of H9c2 cells showed shrinkage and death due to oxidative stress induced by 600µM H<sub>2</sub>O<sub>2</sub>. 24hrs exposure of quercetin (up to 100 µM) on H9c2 cells had no significant effect on viability. 48hrs exposure of quercetin (range 1-100µM) on H9c2 cells decreased viability in a dose dependent manner. Whereas, 72hr exposure significantly decreased the viability of H9c2 cells with higher concentrations of quercetin (i.e. 100 µM and 30 µM) (\*\*p < 0.01 vs Control). In summary, quercetin has a significant protective effect against H<sub>2</sub>O<sub>2</sub> induced cell death. Reduced ERK phosphorylation may have protective effect on H9c2 cells. On the other hand, prolonged exposure with higher quercetin concentrations induced cell death.

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