

Study on the effects of grape extracts in muscle and endothelial cells using a  
combination of molecular methods

**ABSTRACT**

For the past twenty years several grape extracts and other grape products such as wine have been the focus of many studies due to their strong antioxidant properties. Several studies show that grape extracts enhance the cellular antioxidant mechanisms differentially depending on their composition. However, the exact mechanism by which the extracts function remains elusive. In the current paper, the administration of grape pomace extract from the local variety "Batiki Tirnavos" in muscle and endothelial cells led to an improvement in their redox status. The extract displayed a capacity to protect the cells against oxidative damage by improving oxidative stress markers, namely increasing glutathione (GSH) levels in cells. The increase in GSH and improvement on oxidative stress markers may be attributed to the extract's ability to affect the levels and/or the activity of several antioxidant enzymes. It was found that the extract induced an increase in the levels of  $\gamma$ -glutamyl-cysteine synthetase (GCS) and the activity of glutathione transferase (GST) in both cell lines. These two enzymes are involved in the metabolism of glutathione. Overall these results suggest that the GSH system plays a critical role in the antioxidant activity of the extract. Regarding the study of grape stem extracts deriving from three different varieties, it was observed that the antioxidant activity in muscle and endothelial cells depends on their qualitative composition of polyphenols. Specifically, various extracts differently affected oxidative stress cell markers even though same concentrations of polyphenols were used. All these fortify the view that specific polyphenols or polyphenolic proportions can affect the antioxidant activity of the extracts. A further analysis on the effect of the extract on muscle cell gene expression showed that several genes were overexpressed, while some were downexpressed. Interestingly, a number of genes displayed over 1,5 fold over- or down-expression. This raises new questions concerning the mechanisms by which an extract acts.