Induced cytoskeletal changes in bovine pulmonary artery endothelial cells by resveratrol and the accompanying modified responses to arterial shear stress

ABSTRACT

Results of our studies show that resveratrol interacts with endothelial cells in vitro to elicit morphological and structural changes; the observed changes support the interpretation that resveratrol acts as a cardioprotective agent.

INTRODUCTION

Background Atherosclerosis and coronary heart disease (CHD) have long been considered major contributors to morbidity and mortality in developed countries. One noted exception is the low mortality of CHD in France, particularly the southwest region. This phenomenon, commonly referred to as the French paradox, may be associated with high consumption of red wine. A negative correlation between CHD and alcohol consumption was first noted 25 years ago, and numerous studies since have confirmed a statistically significant inverse relationship between these two factors. In vivo studies have shown that wine consumption, particularly red wine, is more effective in the prevention of CHD not seen with other forms of alcoholic beverages. Accordingly, it has been postulated that naturally occurring components in wine might afford or contribute to its enhanced protection against CHD by targeting sites that participate in the etiology of CHD, including soluble blood components (LDL), cellular blood elements (platelets), or the vasculature itself (endothelium). Siemann and Creasy proposed that trans-resveratrol, a tri-hydroxy stilbene, in red wine exhibits cardioprotective properties and can inhibit LDL oxidation, suppress smooth muscle proliferation, induce nitric oxide synthase expression and block collagen-induced aggregation responses in washed platelets. However, relatively few studies have been performed on the effects of resveratrol on vascular components such as the endothelial cells, which are known to play a critical role in maintaining the integrity and functioning of the vascular endothelium. Homeostasis of the vascular endothelium, both with respect to metabolic and physiologic activities, can be affected by overall nutritional status and by specific ingredients in the diet. The aims of the present study were to determine changes resulting from resveratrol:endothelial cell interaction. We observed that resveratrol induced significant cellular and biochemical changes in endothelial cells, which were accompanied by altered functional responsiveness to conditions simulating arterial flow. Since previous studies have shown several signaling molecule changes during reorganization of the endothelial cell cytoskeleton accompanying arterial shear stress, we evaluated the same set of biochemical parameters in resveratrol-treated cells. Use of selective signaling pathway inhibitors allowed the demonstration that the cytoskeletal changes elicited by resveratrol depended on intracellular calcium and tyrosine kinase activity changes, and also appeared to be linked to integrity of actin microfilaments and microtubule network. Resveratrol treatment also led to activation of ERK1/2 MAP kinase, similar to changes induced by shear. Thus resveratrol may act by a mechanism(s) closely resembling that triggered by shear stress.

CONCLUSION

Conclusions Our studies suggest that resveratrol interacts with endothelial cells in vitro to elicit morphological and functional changes. Specifically,

resveratrol induced an elongated shape, interspersed with long, tortuous projections, in cultured BPAEC. Treated cells resisted detachment from the plastic coverslips under simulated arterial shear stress conditions. These results, combined with data from our previous studies, provide additional support for the notion that resveratrol acts as an anti-atherosclerotic agent. Whether these findings can be extrapolated to humans require further study.