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A Total Red Wine Polyphenolic Extract Prevents a Pathological Phenotype Manifested on Cardiomyocytes Isolated from Rats with Nutritionally-induced Metabolic Syndrome

GÉRARD CROS, LUCAS ANDRÉ, CATHERINE OIRY, ELODIE LE SCANF, SANTIAGO ZALVIDÉA, CÉCILE CASSAN, OLIVIER CAZORLA, RICHARD MAGOUS, PIERRE-LOUIS TEISSÈDRE and SYLVAIN RICHARD

ABSTRACT *Isolated cardiomyocyte contractility was explored in a model of metabolic syndrome (the fructose-fed rat) and the effect of a treatment by a total red wine polyphenolic extract (RWPE) determined. Fructose-enriched diet impaired cardiomyocyte maximal shortening and velocities of contraction and relaxation, while RWPE was able to prevent those changes. Those studies suggest that red wine polyphenols are able to prevent the development of a cardiac phenotype commonly observed at an early stage of heart failure.*

Introduction

We have found in earlier research that a total red wine polyphenolic extract (RWPE) was able to prevent hypertension, cardiac hypertrophy and high production of cardiac reactive oxygen species in rats fed a high-fructose (60%) diet, a model of metabolic syndrome (Al-Awwadi *et al.*, 2004). Using echocardiographic analysis, we also explored *in vivo* the myocardial structure and function in this model, but found no significant change (not illustrated). However, we have recently found that cardiomyocyte contractility can be impaired in the absence of *in vivo* detectable underlying cardiomyopathy, cardiomyocytes developing a phenotype commonly observed at an early stage of heart failure when rats are chronically exposed to carbon monoxide, which was associated with decreased antioxidant enzyme activities (Andre *et al.*, 2010), suggesting a pathophysiological role for oxidative stress in its development. We therefore hypothesized that cardiomyocytes from fructose-fed rats may develop a similar impairment and determined the possible effect of RWPE on the contractility of cardiomyocytes from rats fed a standard or a fructose-enriched diet.

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Material and Methods

Rats were fed for eight weeks using a commercially available standard rat chow (CTL) or a fructose-enriched food (HFr) and subdivided into two groups administered (gavage) daily either with the same RWPE under the form of an aqueous suspension (CTL + RWPE or F + RWPE groups) or with an equivalent amount of water (CTL or HFr groups). High-fructose diet was obtained and cardiomyocyte contractility determined as previously indicated (Al-Awwadi *et al*., 2004; Andre *et al*., 2010). The origin and dose of RWPE were identical to those used in our previous study (Al-Awwadi *et al*., 2004). The dose of RWPE (21 mg/kg) was calculated as the amount of polyphenols intake corresponding to the consumption of 500 ml/day of the same red wine by a 70 kg human.

Results

The various parameters of cell contraction are shown in Figure 1A–C. Sarcomere Length Shortening (SLS) (Figure 1A) and velocities of contraction (Figure 1B) or relaxation (Figure 1C) were decreased in HFr as compared to CTL groups. In CTL animals, RWPE induced a decrease in relaxation velocity (Figure 1C). In HFr + RWPE animals, fructose-enriched diet-induced changes of cell contractility were prevented (Figure 1A–C).

Discussion and Conclusion

A fructose-enriched diet impaired cardiomyocyte maximal shortening and velocities of contraction and relaxation, indicating that an imbalanced nutrition may induce a

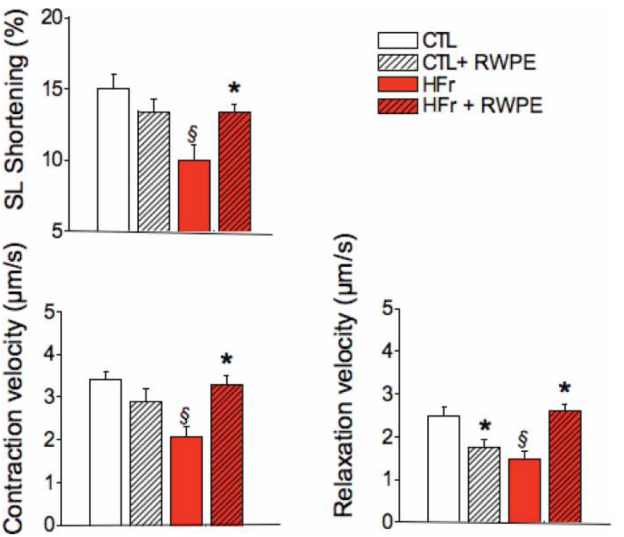


Figure 1. Effect of high-fructose (60%) feeding and red wine polyphenolic extract (RWPE) on rat cardiomyocyte contractility.
Rats were fed for eight weeks either with control (CTL) or high-fructose (Hfr) diet and treated by a daily administration (gavage) of a suspension of RWPE (21 mg/kg) or the corresponding amount of water (10 ml/kg). (§) indicates a significant difference ($p < 0.05$) as compared to the CTL group. (*) indicates a significant difference as compared to the corresponding RWPE-untreated group.

pathological phenotype resembling that of an early stage of heart failure as determined at the cell level.

Although RWPE, used at a dose corresponding to the consumption of 500 ml red wine rich in polyphenols by a 70 kg human, had no apparent effect on the general feature of the animals, our preliminary data indicate that it decreased cardiomyocyte relaxation velocity, suggesting a possible interference of red wine polyphenols with cytosolic calcium handling.

In HFr-fed animals, RWPE prevented fructose-induced functional changes. Whether this effect is linked to its antioxidant effect or to some other cellular mechanisms (e.g. modulation of calcium handling) should be determined.

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