Red grape extracts protective effects on endothelial progenitor cells function and improvement of their polyphenols bioavailability

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Purpose

Maintenance of endothelial integrity and function are greatly affected by circulating endothelial progenitor cells (EPC) number and functional activities. Compounds that can prevent or ameliorate EPC dysfunction are of special clinical interest. Grapes are receiving growing attention as material for potential drug formulation due to the high polyphenolic content. However, polyphenols positive health effects strongly depend on their bioavailability.

Aim of this work was to evaluate the ability of Grape Skin extract (GSE) and Seeds extract (SE) to protect EPC from oxidative stress induced by hyperglycemia (HG) compared to red wine (RW) and to enhance polyphenols absorption across the intestinal epithelium.

Methods

Human EPC were cultured from peripheral blood and characterized by the presence of double positive cells for Dil-Ac-LDL uptake and lectin binding and by expression of cell surface markers. Dry extracts from fresh vegetal material and RW were obtained using Sangiovese grape variety (doc-Montecucco, Italy). Total polyphenols were determined using the Folin-Ciocalteau micro method. EPC were incubated with different concentration of total polyphenols content (5 µg, 50 µg, 150 µg) of GSE, SE and RW. Cell viability, migration and reactive oxygen species (ROS) production were assaysed using the tetrazolium salt reduction (WST-1) assay, modified Boyden chamber assay and with a fluorescent probe CM-H2DCFDA, respectively.

Intestinal red grape polyphenols permeation were tested by Ussing-type chamber in the absence or presence of 1% (w/w) of the quaternary ammonium-chitosan conjugates polymer (N+(60)-Ch).

Results

Effects of SE, GSE and RW on EPC viability. (A) Viabe

Effects of SE, GSE and RW on EPC migration and adhesiveness. Pre-incubation of EPC with 150 µg/ml of drug in SE, GSE and RW for 2 hours prevent the negative effect induced by 3 days of high glucose exposure (HG, 25 mM). (n=6, means ± SD, P<0.05 vs Control and P<0.01 vs HG). (B) Representative image of EPC treated with 150 µg of SE, GSE and RW in the presence of HG levels.

Effects of SE, GSE and RW on ROS production in EPC. Incubation of EPC with 150 µg/ml of GSE and RW for 2 hours induced a significant reduction in intracellular ROS generation compared with cells exposed to high glucose levels (HG) (n=6, means ± SD, P<0.01 vs Control and P<0.01 vs HG).

Conclusions

These results suggest that red grape components are a potential compounds to prevent endothelial dysfunction via EPC amelioration, and that the use of S-(60)-Ch chitosan derivate can promote the absorption of polyphenols across the intestinal epithelium, to guarantee their bioavailability and then their potential therapeutic value in atherosclerosis, as well as in endothelial dysfunction associated with diabetes.

Conflicts of interest: none