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Therapeutics with β -Caryophyllene nanoemulsions for Pulmonary Arterial Hypertension

Abstract: Our research group has studied animal models of pulmonary arterial hypertension (PAH), which is an incurable disease characterized by increased pulmonary vascular resistance (PVR), right ventricular failure, and premature death. Compounds with vasodilatory characteristics, such as β -caryophyllene, extracted from the essential oils of many plants, could be promising therapeutics for PAH. We studied the effects of free and nanoemulsion of β -caryophyllene in the redox state and heart function of rats with PAH. Male Wistar rats (170g, n=6/group) were divided into four groups: control (CO), monocrotaline (MCT), monocrotaline + β -caryophyllene (MCT-Bcar) and monocrotaline + nanoemulsion with β -caryophyllene (MCT-Nano). PAH was induced by MCT (60 mg/kg i.p.) and, 7 days later, treatment with β -caryophyllene or nanoemulsion (by gavage, 176 mg/kg/day), or vehicle was given for 14 days. Echocardiographic and hemodynamic measurements were performed and after, rats were killed by decapitation. Right ventricle (RV) was removed for morphometry, and lungs to evaluate oxidative stress (lipid peroxidation, xanthine oxidase, NADPH oxidase), antioxidant enzymes, total sulphydryl groups, nitric oxide synthase (NOS) activity and endothelin-1 receptors A (ETA-R) and B (ETB-R) expression. It was observed RV hypertrophy, accompanied by an increase in PVR and RV diastolic and systolic pressures (RVSP and RVEDP, respectively) and in mean pulmonary arterial pressure (mPAP) in the MCT group. Treatment with both, free and in nanoemulsion β -caryophyllene significantly ($P < 0.05$) reduced RV hypertrophy, mPAP, RVSP and lung lipid peroxidation. The reduction in RVSP was more pronounced in the MCT-Nano group. Moreover, RVEDP decreased only in the MCT-Nano group. These treatments also increased superoxide dismutase, catalase and NOS activities and decreased ETA-R and ETB-R expressions. Both free and nanoemulsion of β -caryophyllene improved mPAP, PVR and oxidative stress parameters. However, β -caryophyllene in nanoemulsion was more effective in attenuating PAH effects, which might represent a promising strategy to treat patients with PAH.

Keywords: β -caryophyllene, nanoemulsion, pulmonary hypertension, endothelial dysfunction

Biography: I am a biologist, with Masters and PhD in the Physiology (UFRGS, Brazil), and post-doctoral fellowship in the University of Manitoba, Canada. I am full professor of Physiology in Brazil. My research interests are on the participation of oxidative stress in the pathogenesis of heart failure, using animal models of myocardial infarction, right ventricle failure, arterial hypertension. I have studied the effect of antioxidant compounds, such as β -caryophyllene, sulforaphane, pterostilbene, boldine, melatonin, in models of heart failure. We have studied the efficacy of nanoemulsions and nanocapsules formulations for the treatment of heart diseases.