Evaluation of the effect of β-Caryophyllene on oxidative stress in BALB/c mice with streptozotocin-induced diabetes

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ABSTRAC

Background. Type 2 diabetes mellitus (T2DM) is a disease characterized by hyperglycemia, hyperlipidemia, and organic insulin resistance. This pathological change in circulating energy levels and the utilization of the energy substrate by central and peripheral tissues contributes to mitochondrial dysfunction where critical cellular pathways such as energy substrate metabolism and reactive oxygen species (ROS) take place. β-caryophyllene (BCP) is an isolated natural bicyclic sesquiterpene, it is a selective agonist of the cannabinoid receptor type 2 (CB2R), which is mainly expressed in the peripheral nervous system. The antioxidant mechanism of β-caryophyllene is linked to its structure since it has double rings, which allows the insertion of free radicals, avoiding the deterioration of the oxidant/antioxidant state. Objective. The present work aimed to evaluate the effect of β-caryophyllene on oxidative stress in a murine model after streptozotocin administration. Methods. BALB / c mice were used to which streptozotocin was administered, as well as β-caryophyllene and glucose levels, catalaza activity, oxidized lipids and nitric oxide levels were determined. Results. Glucose levels, catalaza activity, and oxidized lipids in the group that was only administered STZ showed a significant increase, while the group that was administered β-caryophyllene significantly decreased glucose levels, as well as oxidized lipids and nitric oxide, on the other hand, catalase activity decreased but was not significant. Conclusion. The β-caryophyllene has a antioxidant effect in reducing the oxidized lipids as well as the nitric oxide generated after the administration of streptozotocin.

Keywords: β-caryophyllene, streptozotocin, diabetes, oxidative stress.

INTRODUCTION

Type 2 diabetes mellitus (T2DM) is a disease characterized by hyperglycemia, hyperlipidemia, and organic insulin resistance. This pathological change in circulating energy levels and the utilization of the energy substrate by central and peripheral tissues contributes to mitochondrial dysfunction where critical cellular pathways such as energy substrate metabolism and reactive oxygen species (ROS) take place. The development of DM after damage to the pancreatic islets is related to the local and systematized induction of oxidative stress. Oxidative stress is an essential factor for the development and progression of diabetes, it is based on the decrease in hyperglycemia and the endogenous antioxidant activities of the organism. The high level of ROS can damage the structure of various biomolecules, including lipids, proteins, and DNA, leading to increased oxidative stress in various diseases in humans, such as DM and neurodegenerative diseases. A sign of oxidative damage to cells and tissues of diabetic patients is lipid peroxidation (LPO). Free fatty acids (FFA) are involved in inducing inducible nitric oxide synthase (iNOS) production and increasing nitric oxide (NO) levels. Recently, the use of antioxidant phytochemicals as adjuvants in the management of diabetes has taken on importance. B-Caryophyllene (BCP) is a natural bicyclic sesquiterpene isolated from clove oil, clove stem oil, cinnamon leaf oil, and pine oil fractions. It has been used as a flavoring agent and as a fragrance ingredient since the 1930s. It is a selective agonist of the cannabinoid receptor type 2 (CB2R), which is mainly expressed in the peripheral nervous system. There are several antioxidants in cells, either enzymatic (superoxide dismutase, glutathione peroxidase, and catalase) or non-enzymatic (such as glutathione and uric acid) as ROS scavengers, to prevent oxidative damage in biological membranes. The antioxidant mechanism of β-caryophyllene is linked to its structure since it has double rings, which allows the insertion of free radicals, avoiding the deterioration of the oxidant/antioxidant state, having protective effects against the variables of hepatic oxidative stress, which avoids a increased levels of ROS and thiobarbituric acid reactive substances (TBARS), and improving the primary hepatic antioxidant defense system. In this sense, the present work aimed to evaluate the effect of β-caryophyllene on oxidative stress in a murine model after the administration of streptozotocin.

METODOLOGY

Animals: For the experiment, 40 male BALB / c mice were used, with an average weight of 22 to 30 gr, from 2 to 3 months of age and with a controlled environment at a temperature of 25 ± 3 ° C and with a cycle of light and darkness of 12:12, with free access to food. They were handled according to the technical specifications for the production, care and use of laboratory animals (Official Mexican Standard NOM-062-ZOO-1999 published by SAGARPA in the Official Gazette of the Mexican Government August 22, 2001).

DM induction: Mice (n = 20) fasted for 16 hours for the administration of a single dose of 160 mg/kg of Streptozotocin (STZ) intraperitoneally. Glucose levels and weight were monitored 10 days after STZ administration.

Administration of β-caryophyllene and vehicle (Treatment): The mice (n = 40) were divided into 4 groups: β-caryophyllene (n = 10) and β-caryophyllene with STZ (n = 10), a daily dose of 10 mg/Kg of β-caryophyllene was administered orally with 150 µl of physiological saline solution, while the control group (n = 10) and STZ (n = 10) were administered 150 µl of vehicle.

Basal glucose: This test was performed once a week, fasting for 4 hours, during 4 weeks of treatment, and blood glucose was determined using a digital glucometer, making a puncture at the end of the tail, at the end of the glucose intake, The corresponding treatment will be administered orally to each group.

Sacrifice and obtaining plasma: All animals were lightly anesthetized with phentobarbital and each mouse was injected subcutaneously with 200 U of heparin and blood was obtained by cardiac puncture. The blood obtained was centrifuged for 10 minutes at 10,000 RPM, separating the plasma, the samples were stored at -80 ° C for the subsequent determination of catalase, lipid peroxidation and nitrites in serum.

RESULTS

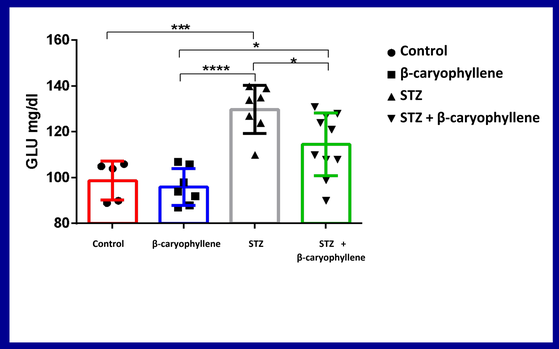

Figure 1. Effect of β-caryophyllene on glucose levels in serum of mice. **Control group**, **β-caryophyllene group** that received 10 mg/Kg of β-caryophyllene, **STZ group** received 160 mg/kg of Streptozotocin and **STZ+β-caryophyllene group** received 160 mg/kg of Streptozotocin and 10 mg/Kg of β-caryophyllene, Data are given as the means ± SE, *p<0.05, ***p<0.01, ****p<0.001

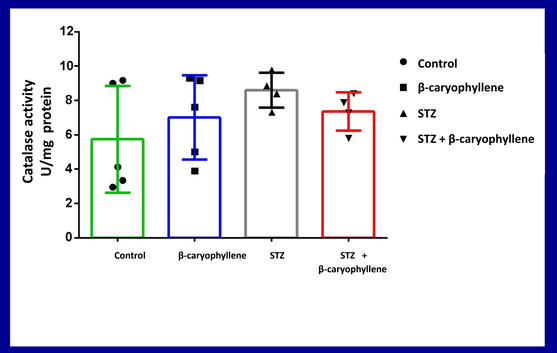

Figure 2. Effect of β-caryophyllene on catalase activity in serum of mice. **Control group**, **β-caryophyllene group** that received 10 mg/Kg of β-caryophyllene, **STZ group** received 160 mg/kg of Streptozotocin and **STZ+β-caryophyllene group** received 160 mg/kg of Streptozotocin and 10 mg/Kg of β-caryophyllene, Data are given as the means ± SE.

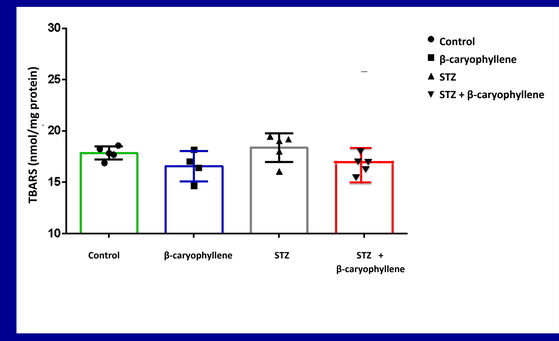

Figure 3. Effect of β-caryophyllene on lipid peroxidation (thiobarbituric acid-reactive substances; TBARS) in serum of mice. **Control group**, **β-caryophyllene group** that received 10 mg/Kg of β-caryophyllene, **STZ group** received 160 mg/kg of Streptozotocin and **STZ+β-caryophyllene group** received 160 mg/kg of Streptozotocin and 10 mg/Kg of β-caryophyllene, Data are given as the means ± SE.

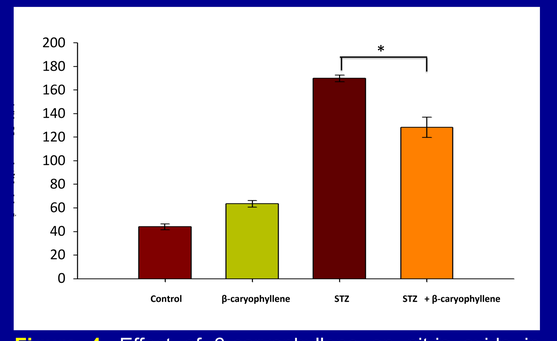

Figure 4. Effect of β-caryophyllene on nitric oxide in serum of mice. **Control group**, **β-caryophyllene group** that received 10 mg/Kg of β-caryophyllene, **STZ group** received 160 mg/kg of Streptozotocin and **STZ+β-caryophyllene group** received 160 mg/kg of Streptozotocin and 10 mg/Kg of β-caryophyllene, Data are given as the means ± SE, *p<0.001.

CONCLUSION

β-caryophyllene reduces glucose levels in mice with streptozotocin-induced hyperglycemia, so this molecule could be an adjuvant treatment in glycemic control

The β-caryophyllene has a antioxidant effect in reducing the oxidized lipids as well as the nitric oxide generated after the administration of streptozotocin, so β-caryophyllene could be a promising molecule as a adjuvant in oxidative disorders that occur in diabetes.

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