Oral administration of carvacrol/β-cyclodextrin complex protects against 6-hydroxydopamine-induced dopaminergic denervation

Camila Tiefensee Ribeiro, Juciano Gasparotto, Lyvia Lintzmaier Petiz, Pedro Ozorio Brum, Daniel Oppermann Peixoto, Alice Kunzler, Helen Tais da Rosa Silva, Rafael Calixto Bortolin, Roberto Farina Almeida, Lucindo José Quintans-Junior, Adriano Antunes Araújo, José Claudio Fonseca Moreira, Daniel Pens Gelain

Abstract

Carvacrol (CARV) presents valuable biological properties such as anti-inflammatory and antioxidant activities. However, pharmacological uses of CARV are largely limited due to disadvantages related to solubility, bioavailability, preparation and storage processes. The complexation of monoterpenes with β-cyclodextrin (β-CD) increases their stability, solubility and oral bioavailability. Here, the protective effect of oral treatment with CARV/β-CD complex (25 µg/kg/day) against dopaminergic (DA) denervation induced by unilateral intranigral injection of 6-hydroxydopamine (6-OHDA - 10 µg per rat) was analyzed, in order to evaluate a putative application in the development of neuroprotective therapies for Parkinson's disease (PD). Pretreatment with CARV/β-CD for 15 days prevented the loss of DA neurons induced by 6-OHDA in adult Wistar rats. This effect may occur through CARV anti-inflammatory and antioxidant properties, as the pretreatment with CARV/β-CD inhibited the release of IL-1β and TNF-α; besides, CARV prevented the increase of mitochondrial superoxide production induced by 6-OHDA in cultured SH-SY5Y cells. Importantly, hepatotoxicity or alterations in blood cell profile were not observed with oral administration of CARV/β-CD. Therefore, this study showed a potential pharmacological application of CARV/β-CD in PD using a non-invasive route of drug delivery, i.e., oral administration.

Keywords:

Carvacrol, β-cyclodextrin, 6-hydroxydopamine, Parkinson's disease