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Medical University
Prof. Dr. Paraskev Stoyanov
Varna, Bulgaria



EFFECT OF *ARONIA MELANOCARPA* FRUIT JUICE ON INDICES OF INFLAMMATION AND FIBROSIS IN A RAT MODEL OF AMIODARONE-INDUCED PNEUMOTOXICITY

Valcheva-Kuzmanova S.¹, G. Stavreva², V. Dancheva³, L. Terziev⁴, M. Atanasova⁵,
A. Stoyanova⁶, V. Shopova³

¹Department of Preclinical and Clinical Pharmacology and Toxicology, Medical University of Varna, ²Department of Experimental and Clinical Pharmacology, Medical University of Pleven, ³Department of Disaster Medicine, Medical University of Pleven, ⁴Clinic of Allergology, University Hospital of Pleven, ⁵Department of Biology, Medical University of Pleven, ⁶Department of Chemistry, Medical University of Pleven

ABSTRACT

The effect of *Aronia melanocarpa* fruit juice (AMFJ) on indices of inflammation and fibrosis was studied in a model of amiodarone (AD)-induced pneumotoxicity in rats. AD was instilled intratracheally on days 0 and 2 (6,25 mg/kg as a 3,125 mg/mL water solution). AMFJ (10 mL/kg) was given orally to rats either from day 1 to day 10, or from day 11 to day 27. Thus, the animal groups were: control, AD, AD+AMFJ (day 1-10), and AD+AMFJ (day 11-27). The rats were sacrificed on day 28. The levels of IL-6 and IL-10 were measured in rat serum as markers of inflammation, and hydroxyproline (HP) level was determined in lung tissue as a marker of fibrosis. AD caused a tendency to elevate IL-6 and decrease IL-10. AMFJ counteracted these effects of AD. In rats from group AD+AMFJ (day 1-10), IL-6 level was significantly lower ($p < 0,05$) than that of AD group, lower ($p < 0,05$) even than the control value. AD significantly increased ($p < 0,05$) HP content in lung homogenate. AMFJ antagonized that effect, and in AMFJ-treated rats HP levels did not differ significantly from the control value. Any AMFJ effects were more prominent in rats that were treated with the juice during the first 10 days after AD instillation. In conclusion, AMFJ reduced the signs of inflammation and could have a protective effect against AD-induced pulmonary fibrosis, especially if administered in the early phase after AD instillation.

Key words: *Aronia melanocarpa* fruit juice, amiodarone, lung, inflammation, fibrosis, rats

INTRODUCTION

Amiodarone (AD) is a very effective antiarrhythmic drug. It causes acute pneumonitis resulting in fatal pulmonary fibrosis (8). *In vivo* and *in vitro* studies have shown that AD is not only directly toxic to lung cells (16) but also could induce oxidative stress and increased production of reactive oxygen species (11,19), activation of alveolar macrophages and cytokine release (4,14,20).

Aronia melanocarpa (Michx.) Elliot (black chokeberry) fruits are extremely rich in phenolic compounds (12): procyanidins, flavonoids (mainly from the subclass of anthocyanins) and phenolic acids (chlorogenic and neochlorogenic). *Aronia* berries possess very high antioxidant capacity (9,12,18). Studies have demonstrated that constituents of *Aronia melanocarpa* fruits (flavonoids in-

cluding anthocyanins) possess anti-inflammatory activity due to the suppression of the release of proinflammatory cytokines such as tumor necrosis factor alpha and interleukins (IL-1beta, IL-6, IL-8) (7,17).

The aim of the study was to investigate the effect of *Aronia melanocarpa* fruit juice (AMFJ) on indices of inflammation and fibrosis in a rat model of AD-induced pulmonary toxicity.

MATERIALS AND METHODS

Experimental substances

Amiodarone hydrochloride (AD) and all other chemicals and reagents were of analytical grade and were purchased from Sigma-Aldrich Company (Germany). The Quantikine Rat IL-6 and IL-10 immunoassay kits were from R&D Systems (USA).

AMFJ was produced from *Aronia melanocarpa* Elliot fruits grown in the Balkan Mountains, Bulgaria. They were handpicked in September, crushed and squeezed. The juice

Address for correspondence

S. Valcheva-Kuzmanova, Dept. of Preclinical and Clinical Pharmacology and Toxicology, Medical University of Varna, 55, Marin Drinov Str., 9002 Varna, Bulgaria
e-mail: stefkavk@yahoo.com