

The encapsulation of ellagic acid increases its hepatoprotective potential in cyclophosphamide induced liver injury model

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Abstract

Introduction: Encapsulation and controlled release of compounds from nanoliposomes rapidly developing strategy for increasing their solubility and enable compounds to reach target tissue [1]. Ellagic acid is a naturally occurring polyphenol, with strong antioxidant potential, that can be found in numerous plants including fruit and nuts [2]. In this study we aimed to evaluate whether the encapsulation of ellagic acid into nanoliposomes would improve its potential in preventing cyclophosphamide-induced liver damage. **Methods:** Experiments were performed on 60 male Wistar rats divided into ten groups of 6 animals, treated daily by an intraperitoneal injection. CP-group received cyclophosphamide in a single dose (200 mg/kg) on the third day; other experimental groups received the same dose of cyclophosphamide and: corn oil (0.2 ml/day) (OCP-group), empty nanoliposomes (10 ml/kg) (NLCP-group), ellagic acid (10 mg/kg) (EACP-group) and encapsulated ellagic acid (10 mg/kg) (EANLCP-group), for 5 days. The remaining five groups served as controls and received for 5 days: saline (0.2 ml/day) (C-group), corn oil (0.2 ml/day) (O-group), empty nanoliposomes (10 ml/kg) (NL-group), ellagic acid (10 mg/kg) (EA-group) and encapsulated ellagic acid (10 mg/kg) (EANL-group). Quantitative evaluation of structural and functional changes of liver was performed by histopathological and biochemical serum analyses and determination of oxidative stress parameters. **Results:** Cyclophosphamide induced severe functional and morphological alterations of liver with disarrangement of hepatic plates caused by vacuolar degeneration and focal apoptosis. Histological damage was most pronounced in periportal areas (Figure 1F). Pathohistological findings were followed by AST, ALP, γ -GT and ALT increase and disturbances of tissue antioxidant status. Application of both forms of ellagic acid ameliorated changes of serum and oxidative damage markers and markedly reversed structural changes of liver tissue induced by cyclophosphamide. Animals that received nanoliposome-encapsulated ellagic acid showed higher degree of recovery than those treated with free form (Figure 1). **Discussion:** Encapsulated ellagic acid was shown to possess stronger antioxidant activity which could be possibly related to its higher stability in nanoliposomes which might prolong the presence of ellagic acid in circulation and could significantly increase its hepatoprotective potential [3].

Image

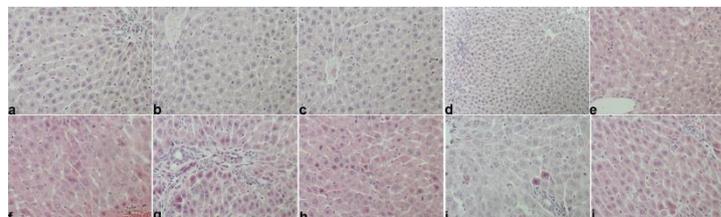


Figure 1. Histological evaluation of liver tissue (HE, 400x) in: (a) C-group; (b) O-group; (c) NL-group; (d) LYC group; (e) ENL group; (f) CP group; (g) OCP-group; (h) NLCP group; (i) EACP group and (j) EANLCP group.

Biography:

Sonja Ilic, associate professor at the Department of Physiology, Faculty of Medicine, University of Nis, is doing the experiments in the fields of experimental medicine, especially in the field of experimental nephrology and hepatology. Her main work is related to the clarification of mechanism of action of different hepato/nephroprotective agents (antibiotics, cytostatic drugs, heavy metals, etc.) in rats. Also, her work is aiming to discover new hepato/nephroprotective agents that can be used in every day clinical practice, such as naturally occurring and/or synthetic antioxidant agents. Her current work involves encapsulation of ellagic acid in nanoliposomes and evaluation of its potential in preventing anticancer drugs-induced liver and kidney damage.

Speaker Publications:

Recent publications

1. Stojiljkovic N, Ilic S, Jakovljevic V, Stojanovic N, Stojnev S, Kocic H, Stojanovic M, Kocic G (2018) The encapsulation of lycopene in nanoliposomes enhances its protective potential in methotrexate-induced kidney injury model. *Oxid Med Cell Longev* 2018:2627917.
2. Yüce A, Atessahin A, Ceribasi AO, Aksakal M (2007) Ellagic acid prevents cisplatin-induced oxidative stress in liver and heart tissue of rats. *Basic Clin Pharmacol Toxicol* 101:345–349.
3. Polce SA, Burke C, França LM, Kramer B, de Andrade Paes AM, Carrillo-Sepulveda MA (2018) Ellagic acid alleviates hepatic oxidative stress and insulin resistance in diabetic female rats. *Nutrients* 10(5). pii:E531.
4. Bala I, Bhardwaj V, Hariharan S, Kharade SV, Roy N, Ravi Kumar MN (2006) Sustained release nanoparticulate formulation containing antioxidant-



ellagic acid as potential prophylaxis system for oral administration. J Drug Target 14(1):27-34.

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