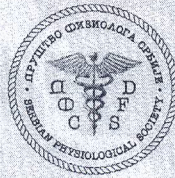


2018

**4th CONGRESS OF PHYSIOLOGICAL SCIENCES OF SERBIA
WITH INTERNATIONAL PARTICIPATION**

Organized by the Serbian Physiological Society



Under the auspices of

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**CURRENT TRENDS IN PHYSIOLOGICAL SCIENCES:
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ABSTRACT BOOK

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PRETREATMENT OF DIABETIC RATS WITH ETHYL PYRUVATE UPREGULATES HMGB1-DRIVEN PROTECTIVE AUTOPHAGY IN THE LIVER

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Oxidative stress, cell damage and cell death underlies the etiology of liver damage/dysfunction in diabetes. High Mobility Group Box 1 (HMGB1) is a nuclear protein that is released from damaged/stressed liver cells during diabetes and contributes to oxidative stress-mediated autophagy and cell death/survival. Since ethyl pyruvate (EP), an HMGB1 release inhibitor, possesses anti-oxidative properties, we have examined whether the pretreatment of diabetic rats with EP, has an effect on HMGB1 release/expression and autophagy in the liver of diabetic rats. Diabetes was induced by streptozotocin (65mg/kg/ip). Pretreated group of diabetic rats (EP+D) started treatment with EP (80mg/kg/daily) three days before diabetes induction, while in the second group (D+EP) treatment started ten days after diabetes induction. In comparison with D+EP group, EP+D group had better glycemic status and higher activity of antioxidative enzymes SOD and CAT in diabetic liver. According to Western immunoblot analyses, EP+D group showed higher expression of extracellular HMGB1 in comparison with D+EP. Consequently, detected increase in HMGB1/RAGE interactions in EP+D group were followed by higher expression of LC3-II, HMGB1/Beclin 1 interaction and activation of autophagy. Expression of LC3-II and HMGB1/Beclin 1 interaction were at the control level in D+EP. Preserved liver morphology in both EP treated groups, observed by electron microscopy, implicated existence of adaptive mechanisms in EP+D group. Further analyses showed that protective autophagy (mitophagy) was enhanced in EP+D group compared with diabetic and D+EP groups. Thus, treatment of diabetic patients with EP may constitute a new strategy for the treatment of diabetes-related tissue injury.

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