



The effect of melatonin on parameters of inflammation and oxidative damage in liver tissue during lipopolysaccharide-induced endotoxemia: an experimental study



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Introduction: Lipopolysaccharide (LPS), as an endotoxin (makes up 70% of the cell wall of gram-negative bacteria), binds to TLR4 receptors of Kupffer's and sinusoidal endothelial cells of the liver, leads to the translocation of NF- κ B into the nucleus, and consequently to the release of pro-inflammatory cytokines (TNF- α and IL-6), which are involved in the cytosolic production of reactive oxygen species - leading to increased oxidative stress.

Melatonin (MLT) is a polypeptide that is synthesized from tryptophan and exhibits anti-inflammatory, antioxidant, antiapoptotic effects, as well as inhibits the synthesis of nitric oxide (NO).

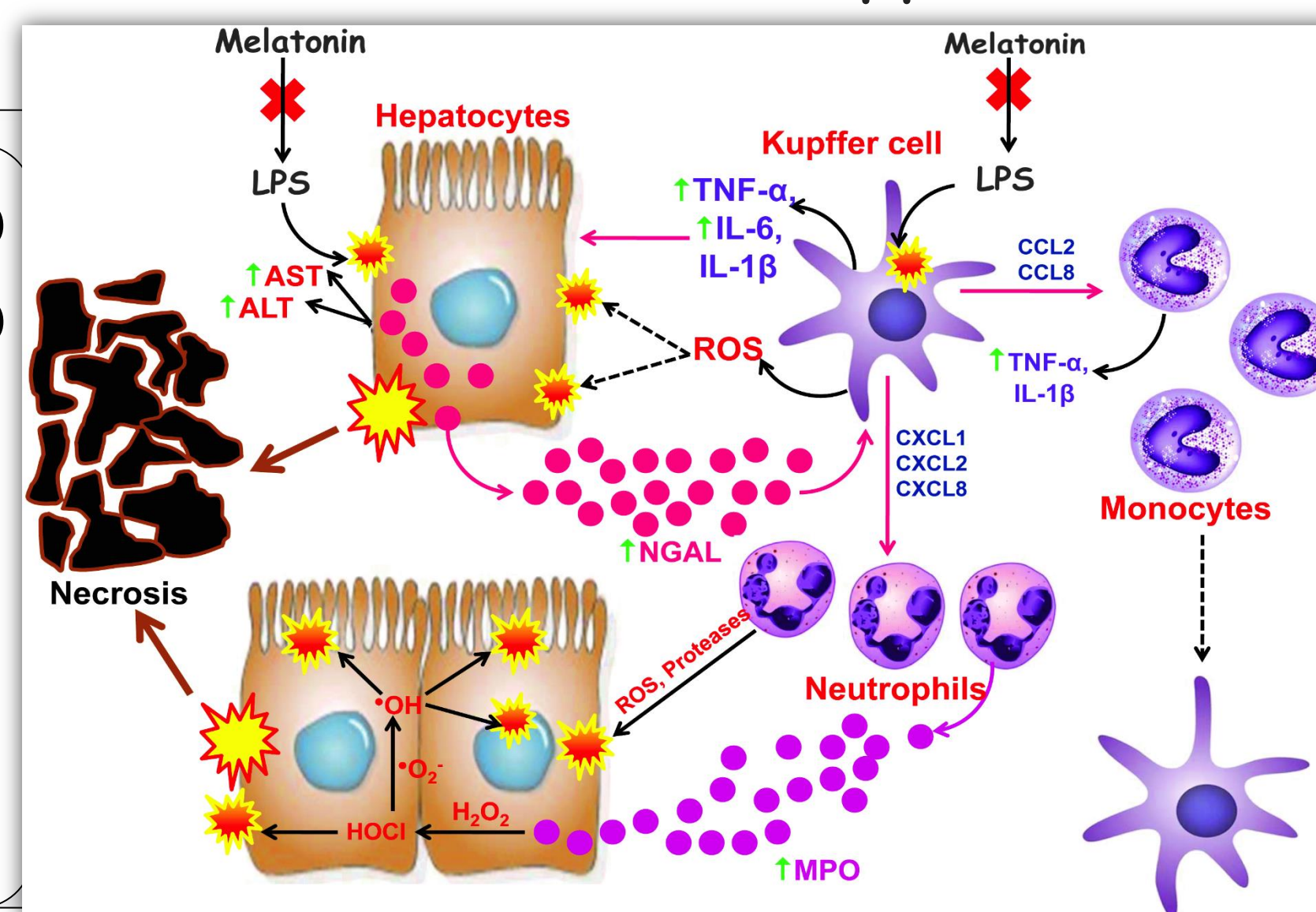
The Aim:

The aim of this research was to evaluate the effect of melatonin in preventing liver damage caused by *Escherichia coli* lipopolysaccharide, by analyzing: parameters of inflammation (nitrates/nitrites - as a measure of NO, NF- κ B and TNF- α), levels of oxidative stress (by monitoring thiobarbiturate-reactive substances-TBARS and carbonyl groups-PCC) and NRF-2 levels - an important defense mechanism against oxidative stress and inflammation, as well as the effects of melatonin supplementation on the investigated parameters.

Material and methods:

Twenty-eight Wistar Albino rats were randomly divided into four groups (n=7) as follows:

- 1) Control group,
- 2) MLT group (50 mg/kg),
- 3) LPS group (10 mg/kg),
- 4) LPS+MLT group.



Results:

In the liver of rats treated with LPS, the concentrations of TBARS, PCC and NO were significantly elevated ($p < 0.001$), while the administration of MLT led to a decrease in the level of these parameters ($p < 0.01$). Treatment of animals with endotoxemia with melatonin (LPS+MLT group) significantly normalized the high levels of TNF- α and NF- κ B compared to the LPS group ($p < 0.01$). It was found that the concentrations of NRF-2 in the liver were significantly elevated in LPS-treated animals ($p < 0.001$).

Conclusions:

This study showed a great hepatoprotective potential of melatonin in endotoxemic rats. During sepsis, in liver tissue, melatonin exerts significant immunomodulatory effects and reduces the intensity of oxidative damage.

References:

- 1) Sokolović DM, Lazarević M, Milić D, Stanojković Z, Mitić K, Sokolović D. Melatonin arrests excessive inflammatory response and apoptosis in lipopolysaccharide-damaged rat liver: A deeper insight into its mechanism of action. Tissue and Cell 2022;79:101904.
- 2) Colunga Biancatelli RML, Berrill M, Mohammed YH, Marik PE. Melatonin for the treatment of sepsis: the scientific rationale. J Thorac Dis 2020;12:S54-S65.

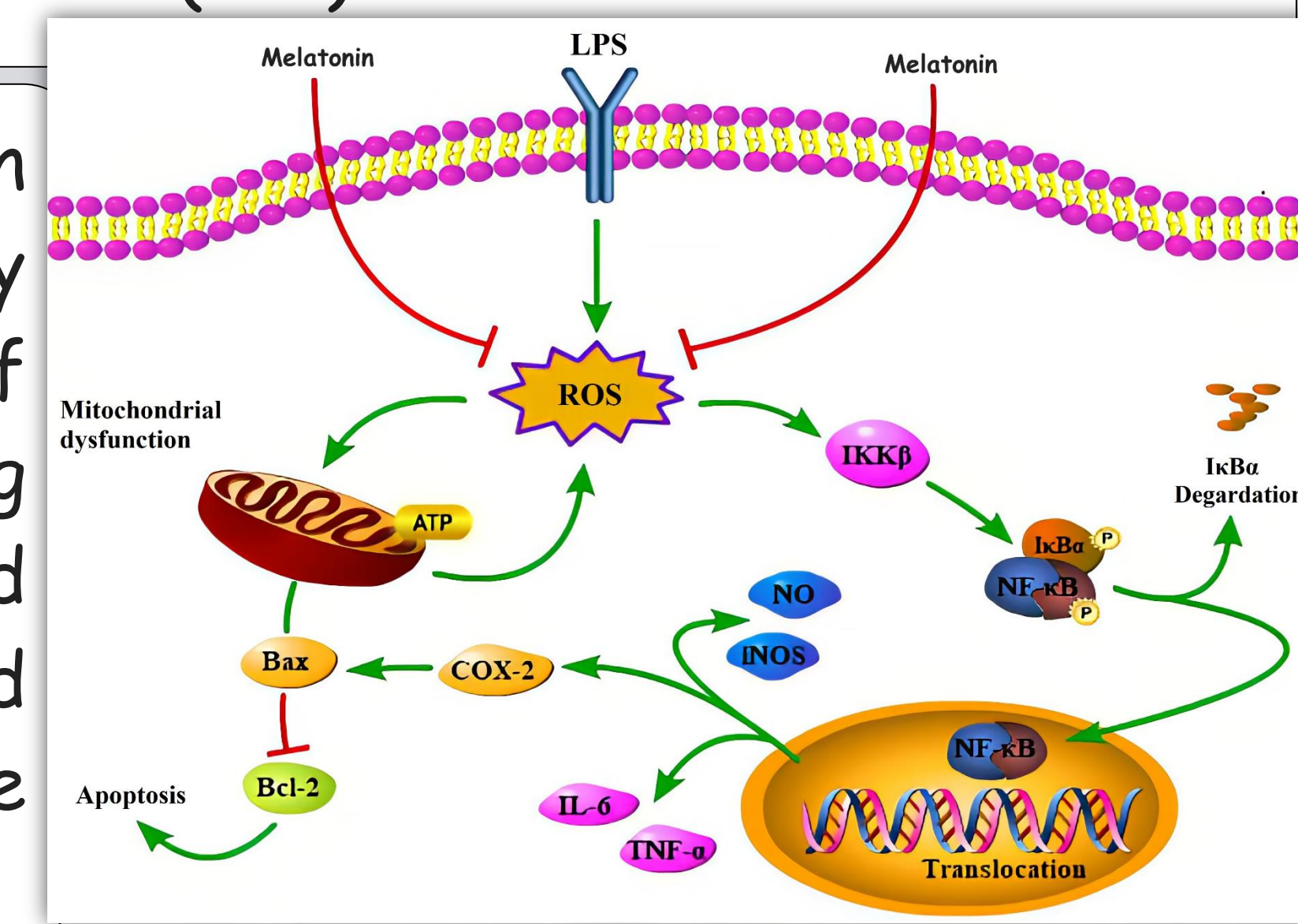


Fig. 1. Effect of melatonin and endotoxemia induced by lipopolysaccharide on the level of tumor necrosis factor (TNF- α) in liver tissue

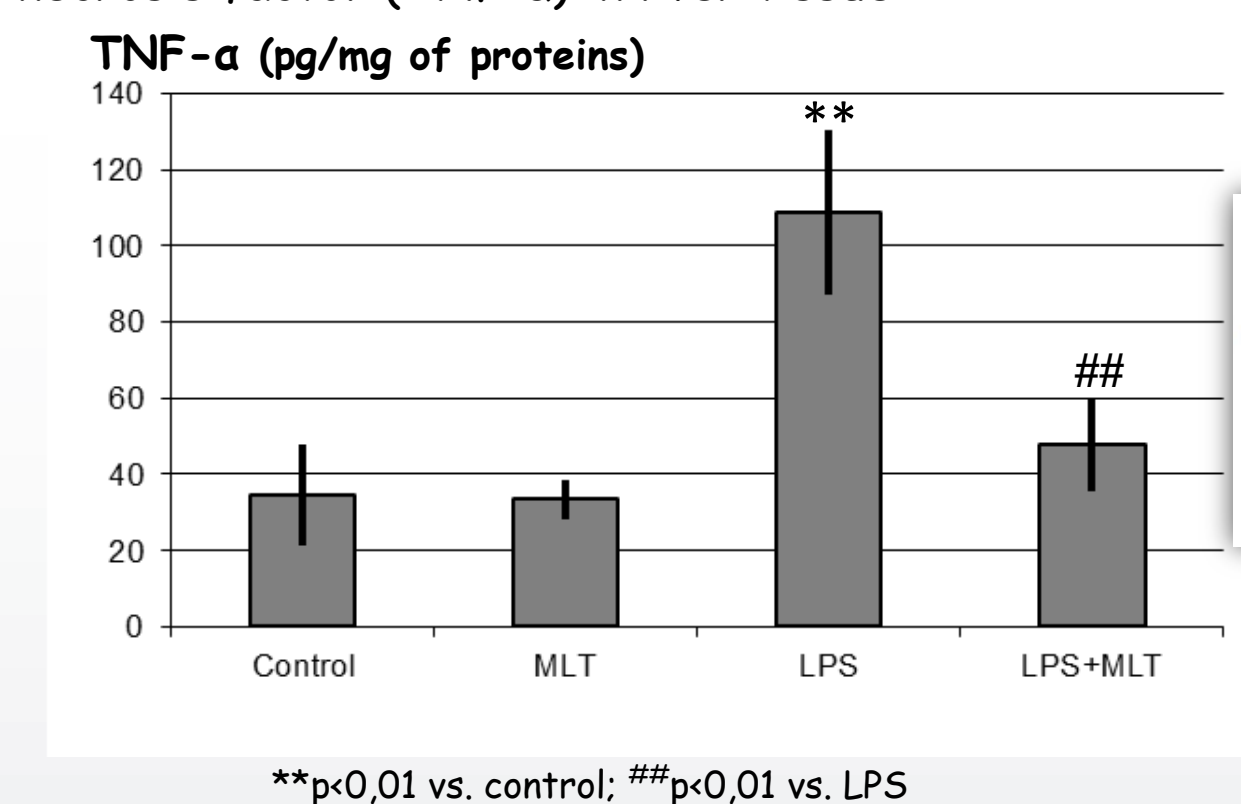


Fig. 2. Effect of melatonin and endotoxemia induced by lipopolysaccharide on the level of nuclear kappa-B (NF- κ B) in liver tissue

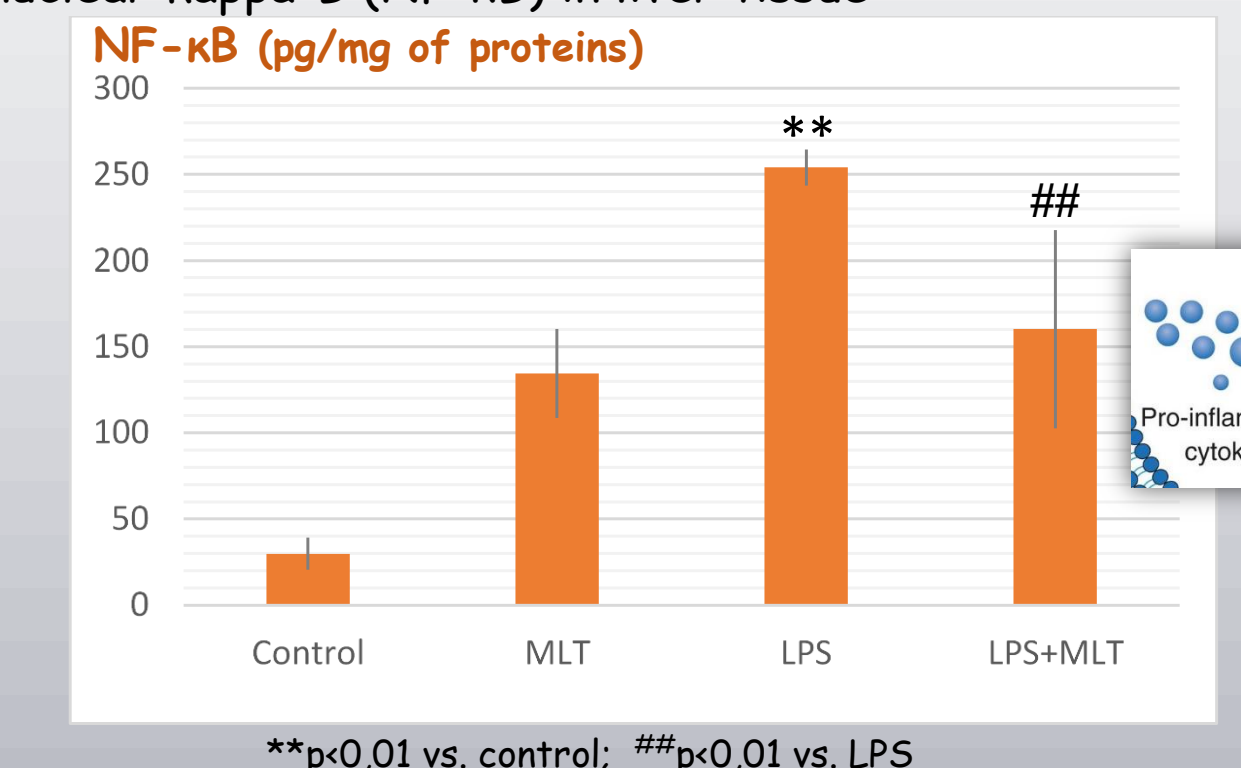
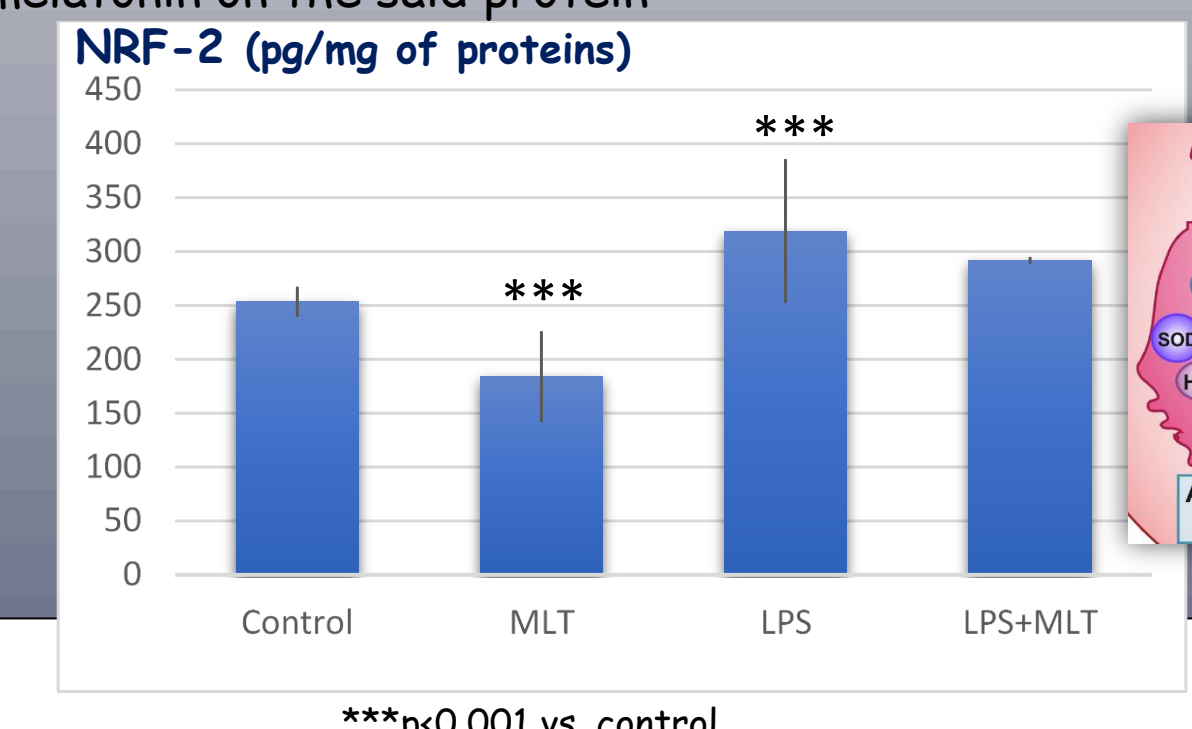


Fig. 3. Concentration of NRF-2 in the liver tissue of rats with endoxemia and the effect of melatonin on the said protein



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