

## Effects of topical NSAIDs on LPS-induced inflammation

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To investigate the effects of topical nonsteroidal anti-inflammatory drugs (NSAIDs) on retinal vascular leakage, and inflammatory markers in endotoxin-induced uveitis (EIU) in rats. EIU was induced in rats by single footpad injection of LPS (350 µg/kg, *Salmonella typhimurium*). Animals were treated according to the ARVO statement for the use of animals in ophthalmology and vision research. Topical indomethacin 0.5% (Indoma<sup>TM</sup>), bromfenac 0.09% (Yelloxa), and nepafenac 0.1% (Nevanaca<sup>TM</sup>) were given before and after LPS injection (four administrations). Twenty-four hours after LPS injection the animals were euthanized and retina and plasma were collected to assess PGE<sub>2</sub> and C-reactive protein (CRP) levels using ELISA. Retinal vascular leakage was assessed by Evans blue extravasation. Twenty-four hours after LPS injection, significant ( $p < 0.01$ ) increases in retinal PGE<sub>2</sub> levels were observed. Plasma CRP levels were significantly ( $p < 0.01$ ) higher in LPS-injected rats compared to control group. The analysis of retinal vascular leakage revealed a significant ( $p < 0.01$ ) decrease after treatment with indomethacin, on the contrary no significant changes were observed after treatment with bromfenac and nepafenac. All NSAIDs tested significantly prevented PGE<sub>2</sub> synthesis with higher effect of indomethacin and bromfenac in comparison to nepafenac. All NSAIDs tested did not affect plasma CRP levels. These results demonstrated that topical treatment with indomethacin, bromfenac, and nepafenac has significant anti-inflammatory effects. However, only indomethacin was able to prevent vascular leakage in LPS-injected rats.