

## THE EFFECT OF NEFERINE ON RETINAL TISSUE IN EXPERIMENTAL DIABETIC RAT MODEL

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**Aim:** To investigate vascular endothelial growth factor (VEGF) and proliferating cell nuclear antigen (PCNA) immunoreactivities, as well as apoptosis and oxidative stress levels in streptozotocin (STZ)-induced diabetic rats, and determine how Neferine affected these parameters.

**Design:** A four-week prospective experimental study

**Methods:** 35 male Sprague Dawley rats aged 8-10 weeks and weighing 200-250 g were divided into five groups of seven. Fasting blood glucose was measured 72 hours after intraperitoneal injection of a single 60mg/kg STZ dose dissolved in 0.4ml (0.1 M) sodium-citrate buffer (pH:4.5) to 21 rats for DM induction, with values >250 mg/dl considered diabetic. Following experimental DM induction, (a) Group 2 (Sham group) received daily intraperitoneal 0.25 ml/kg 0.9% normal saline throughout the experiment; (c) Group 4 (DM plus Bevacizumab) received a single intraperitoneal 0.01mL (2.5 mg/kg) Bevacizumab injection, followed by daily intraperitoneal 0.25 mL/kg 0.9% normal saline throughout the experiment; and (d) Group 5 (DM plus Neferine) received daily intraperitoneal 4 mg/kg Neferine throughout the experiment. While Group 1 (control) received no treatment, normal healthy rats in Group 3 (Neferine) received daily intraperitoneal 4 mg/kg Neferine throughout the experiment. The total antioxidant capacity (TAS) and total oxidative stress (TOS) levels in serum and eye tissue homogenates were evaluated using ELISA. Immuno-histochemical staining for PCNA and VEGF was performed, and apoptotic cells were determined using TUNEL method.

**Results:** In comparison to group IV, group V had significantly higher TAS and lower TOS in serum and eye tissue homogenates ( $p<0.05$  for both). Despite significantly lower VEGF levels and apoptotic cells ( $p<0.05$  for both), there was no significant change in PCNA levels in group V ( $p>0.05$ ).

**Conclusions:** DM was associated with significantly decreased TAS in retinal tissue, increased TOS and apoptotic cells, as well as VEGF and PCNA immunoreactivities. Neferine altered parameters other than PCNA in the opposite direction, demonstrating a reductive effect on DM.