

## Role of nicotine during diabetic macular edema development

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Diabetic macular edema (DME) represents the major cause of visual loss in diabetes patients. It is characterized by retinal thickening in the macular area due to breakdown of the blood-retinal barrier (BRB) [1]. By altering blood vessels supplying retina, hyperglycemia triggers tissue hypoxia. The primary response to latter is mediated by hypoxia-inducible factors (HIFs) which in turn promote vascular endothelial growth factor (VEGF) expression. The most important psychoactive compound in cigarette smoke, nicotine (NT), binds nicotinic cholinergic receptors (nAChRs) which are widely distributed in several human tissues, including retinal pigmented epithelium (RPE) [2]. Until now, little is known about risk factors linked to cigarette smoke inducing DME development. In the present study, we have evaluated NT effect in an *in vitro* model of outer BRB following exposure to hyperglycemic/hypoxic insult mimicking DME microenvironment. Our results have suggested that NT deeply impacts on outer BRB integrity by increasing its permeability. To investigate the molecular mechanisms involved in negative effect of this compound, we have analyzed HIF/VEGF system in cells exposed to hyperglycemic/hypoxic damage. NT treatment induced upregulation of HIF-1 $\alpha$ /HIF-2 $\alpha$ , VEGF mediated through activation of MAPK/ERK1/2 pathway. In conclusion, all this data have suggested a unfavorable role of this psychoactive agent in smokers DME affected.

### References

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### Keywords

Diabetic macular edema, hyperglycemia, hypoxia, nicotine, hypoxia-inducible factors, vascular endothelial growth factor