

# **Role of Avastin in Anterior Segment of the Eye**

**Essay**

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# دور الأفاستين فى علاج أمراض الجزء الأمامى للعين

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THIS WORK IS DEDICATED TO  
MY FATHER  
PROF. DR. MAHMOUD ADAM  
THE BOTANY PROFESSOR IN FACULTY OF  
SCIENCE  
ASSIUT UNIVERSITY  
&  
MY DEAR MOTHER

بِسْمِ اللَّهِ الرَّحْمَنِ الرَّحِيمِ

"قَالُوا سُبْحَانَكَ لَا عِلْمَ لَنَا إِلَّا

مَا عَلَّمْتَنَا إِنَّكَ أَنْتَ الْعَلِيمُ

الْحَكِيمُ"

البقرة : ٣٢

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## LIST OF ABBREVIATIONS

- **5-FU** 5-Fluorouracil
- **AH** aqueous humour
- **AMD** age-related macular degeneration
- **Ang** Angiopoietins
- **BCVA** Best-corrected visual acuity
- **bFGF** basic fibroblast growth factor
- **BRVO** branch retinal vein occlusion
- **CAT-102** Cambridge Antibody Technology
- **CNV** corneal neovascularization
- **CRVO** central retinal vein occlusion
- **CSP** compounded sterile products
- **DR** diabetic retinopathy
- **EC** endothelial cells
- **ECM** extracellular matrix
- **EGF** Epidermic Growth Factor
- **EPC** endothelial precursor cells
- **Epo** Erythropoietin
- **FA** Fluorescein angiography
- **FDA** Food and Drug Administration
- **F-dUMP** 5-fluoro-2'-deoxyuridine 3'-phosphate
- **FGF** fibroblast growth factor
- **flt-1** fms-like tyrosine kinase-1
- **HB-EGF** heparin binding epidermal growth factor



- **HIF-1 $\alpha$**  Hypoxia-inducible factor-1 $\alpha$
- **ICB** intracameral bevacizumab
- **IGF-1** insulin-like growth factor
- **IOP** intraocular pressure
- **IVB** intravitreal bevacizumab
- **IVT** Intravitreal
- **KDR** Kinase inserting domain-containing receptor
- **LECs** lymphatic endothelial cells
- **MMC** Mitomycin C
- **MMPs** Matrix metalloproteinases
- **NOS** Nitric oxide synthetase
- **NV** neovascularization
- **NVG** Neovascular glaucoma
- **NVM** neovascular membrane
- **PBK** pseudophakic bullous keratopathy
- **PBS** Phosphate-buffered saline
- **PDGF** Platelet derived growth factor
- **PDR** proliferative diabetic retinopathy
- **PDT** Photo dynamic therapy
- **PEDF** pigment epithelium-derived factor
- **PKP** penetrating keratoplasty
- **PRP** panretinal photocoagulation
- **RPE** Retinal pigment epithelium
- **SGF** Simulated gastric fluid
- **TGF- $\beta$**  transforming growth factor beta
- **TGF- $\beta$  $^2$**  tumor growth factor

- **TNF- $\alpha$**  tumor necrosis factor-alpha
- **tPA** tissue plasminogen activator
- **TSP- $\gamma$**  thrombospondin - $\gamma$
- **uPA** urokinase-type plasminogen activator
- **UV-B** ultraviolet light
- **VA** Visual acuity
- **VEGF** vascular endothelial growth factor
- **VEGFR** VEGF receptor
- **$\alpha$ -SMA** alpha-smooth muscle actin

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## Introduction

Ocular neovascularization (NV) is the primary cause of blindness in a wide range of ocular diseases, such as diabetic retinopathy (DR), age-related macular degeneration (AMD), retinopathy of prematurity, central and branch retinal vein occlusion (CRVO and BRVO), infectious keratitis, trauma and various inflammatory ocular diseases. The avascular feature of certain ocular compartments, including the cornea, lens, vitreous and outer retina, is a unique anatomical characteristic to meet the requirement for normal visual function.<sup>1</sup>

In healthy adults, the fully developed ocular vascular system is in a quiescent status (also known as homeostasis), which is tightly controlled by the balance between the angiogenic stimulating factors, such as vascular endothelial growth factor (VEGF) and angiogenic inhibitors, such as pigment epithelium-derived factor (PEDF).<sup>2</sup>

The homeostasis in the eye is important to keep the structural and functional integrity of the ocular vascular system. In a variety of pathological conditions, such as hypoxia, ischemia, inflammation, infection and trauma, the balance between angiogenic stimulators and angiogenic inhibitors is disturbed, leading to the formation of new vessels.<sup>3</sup> The abnormal growth of new vessels into the avascular compartments will cause disturbance of light transportation. Moreover, these new vessels have abnormal cellular components and lack basement membrane and pericytes, and thus, are very fragile, leaking, and susceptible to hemorrhage. The resultant hemorrhage or accumulation of blood in ocular

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cavities, such as anterior chamber and vitreous, leads to the further blockage of light transportation and decrease of visual acuity.

In addition, the leakage and accumulation of fluid, protein and lipid result in edema and exudation, which will cause visual damage by decreasing corneal transparency and impairment of the structure and function of retinal neurons.<sup>1</sup>

Among the different tissues in the eye, the retina, choroid and cornea are the most frequent sites of ocular NV. Iris NV is also seen in severe ischemic ocular diseases and neovascular glaucoma. The exact mechanism underlying the pathogenesis of ocular NV is not yet well understood, and as a consequence, no specific and satisfactory therapy is available for ocular NV at present, although laser treatment does show some effects on the control of retinal and choroidal neovascularization (CNV). In the past decade, a number of studies provided increasing evidence demonstrating that the imbalance between the angiogenic stimulating factors and angiogenic inhibitors is the major causative contributor to the angiogenesis induced by various insults, such as hypoxia, ischemia, inflammations or tumors.<sup>2</sup>

Angiogenic inhibitors alone or in combination with other existing therapies are, therefore, promising in the treatment of ocular NV in the near future. The recent progress in the studies on the mechanisms and treatment of ocular NV are focusing on the implication and therapeutic potential of endogenous angiogenic inhibitors in ocular NV.<sup>3</sup>