



COLLAGEN CROSS-LINKING FOR THE TREATMENT OF INFECTIOUS KERATITIS

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٢٠١٦

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بِسْمِ اللَّهِ الرَّحْمَنِ الرَّحِيمِ

قالوا

سُبْحَانَكَ لَا عِلْمَ لَنَا
إِلَّا مَا عَلَّمْتَنَا إِنَّكَ أَنْتَ
الْعَلِيمُ الْعَظِيمُ

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List of Abbreviations

AC	Anterior champer
AK	Acanthamoeba keratitis
BAC	Benzalkonium chloride
BB	Big bubble
BCVA	Best corrected visual acuity
BZ	Descemet's membrane banded zone
CACXL	Contact lens-assisted Collagen Cross-linking
CFU	Colony forming units
CH	Corneal hysteresis
CL	Contact lens
cm	Centimetres
CRF	Corneal resistance factor
CT	Corneal thickness
CXL	Collagen cross-linking
DL	Dua's layer
DM	Descemet's membran
EBM	Epithelium basement memberane
EC	Endothelial cells
ECD	Endothelial cell density
EDTA	Ethylenediaminetetraacetic acid
EI-CXL	Epithelial island cross-linking
g	Grams
HSV	Herpes Simplex virus
ICRS	Intra-corneal ring segment
INTACS	Intra-stromal Corneal Segments
IOP	Intraocular pressure

IVCM	Invivo Laser Scanning Conofocal Microscopy
J	Joules
KC	Keratoconus
LASIK	Laser insitu karatomileuses
LEC	Limbal epithelial cells
LogMAR	Logarithm of minimum angle of resolution
mg	Milligrams
min	Minutes
ml	Millilitres
mm	Millimetres
MMP	Matrix metalloproteinases
mol	Mole
µm	Microns
NBZ	Descemet's membrane non-banded zone
Nm	Nanometres
OCT	Optical Coherence Tomography
PACK-	Photo-activated Chromophore for keratitis-CXL
PBK	Pseudophakic bullous keratoplsty
Pixl	Photo-refractive intrastromal cross linking
PLE	Post-LASIK ectasia
PKP	Penetrating keratoplasty
PMD	Pellucid marginal degeneration
PRK	Photo-refractive Keratectomy
RNA	Ribonucleic acid
SDA	Saburaud's Dextros agar
SH	Second Harmonic
SimLC	Simultaneous Topography-guided PRK and CXL

 List of Abbreviations

TKP	Therapeutic keratoplasty
TM	Trabecular meshwork
UCVA	Uncorrected distant visual acuity
UV	Ultraviolet
VA	Visual acuity

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Abstract

Microbes develop resistance to antibiotics as a result of chromosomal mutation, inductive expression of latent chromosomal genes, or exchange of genetic material via transformation, bacteriophage transduction, or plasmid conjugation. Some microbial keratitis resistant to the newest antibiotics have been recently described.

A considerable amount of research is directed toward developing newer antibiotics or defining alternative methods of treatment. Corneal degradation and melting occurs when specific proteinases are upregulated after corneal damage. These matrix metalloproteinases are synthesized either in the keratocytes (matrix metalloproteinase 2) or by corneal epithelial cells (matrix metalloproteinase 9) and are also responsible for delayed epithelial wound healing.

Corneal collagen cross-linking (CXL) is a novel technique used for the treatment of keratoconus (KC) and postoperative ectasia using ultraviolet-A (UV-A) and riboflavin to increase the biomechanical strength of the cornea thus giving it possibilities to block the progression of KC.

Key words: **IVCM:** Invivo Laser Scanning Conofocal Microscopy,
J: Joules, **KC:**Keratoconus

INTRODUCTION

Microbial keratitis is an infection of the cornea that is associated with a risk of permanent visual impairment.^{1,2} It can be caused by bacteria, virus, fungus, protozoa and parasites. The common risk factors for infectious keratitis include ocular trauma, contact lens wear, recent ocular surgery, pre-existing ocular surface disease, dry eyes, lid deformity, corneal sensation impairment, chronic use of topical steroids and systemic immunosuppression.³

Most community-acquired cases of microbial keratitis resolve with empiric treatment using broad-spectrum topical antimicrobials. If diagnosis and initiation of appropriate antimicrobial treatment are delayed, it has been estimated that only 50% of the eyes will heal with good visual outcome.⁴ However, the emergence and spread of antimicrobial-resistant organisms remain serious clinical and public health concern which is associated with a worse clinical presentation and marked visual impairment.^{5:8}

Microbes develop resistance to antibiotics as a result of chromosomal mutation, inductive expression of latent chromosomal genes, or exchange of genetic material via transformation, bacteriophage transduction, or plasmid conjugation. Some microbial keratitis resistant to the newest antibiotics have been recently described.^{9,10}

A considerable amount of research is directed toward developing newer antibiotics or defining alternative methods of treatment. Corneal degradation and melting occurs when specific proteinases are upregulated after corneal damage. These matrix metalloproteinases are synthesized either in the keratocytes (matrix metalloproteinase 2) or by corneal epithelial cells (matrix metalloproteinase 9) and are also responsible for delayed epithelial wound healing.^{11,12}

Corneal collagen cross-linking (CXL) is a novel technique used for the treatment of keratoconus (KC) and postoperative ectasia using ultraviolet-A (UV-A) and riboflavin to increase the biomechanical strength of the cornea thus giving it possibilities to block the progression of KC. It has been shown also that CXL demonstrates excellent antimicrobial efficacy against a variety of common pathogens in vitro. The combination of riboflavin and UVA (280-370 nm) damage nucleic acids by direct electron transfer, production of singlet oxygen, and generation of hydrogen peroxide with formation of hydroxyl radicals in a dose-dependent manner. The evidence that CXL can effectively treat clinical microbial keratitis and arrest the progression of corneal melting, however, is limited.¹

AIM OF THE STUDY

To review the literature about Corneal Cross-Linking with Photoactivated riboflavin in the management of infectious keratitis associated with corneal melting.

ANATOMY OF THE CORNEA

The cornea is the transparent, anterior one-sixth of the eyeball, which along with the precorneal tear film forms the major refracting surface of the eye and serves as a barrier between the environment and the inside of the eye. Microscopically the cornea is classically composed of 5 layers from front to back **(Figure1)**: 1-Epithelium 2-Bowman's layer 3-Stroma 4-Descemet's membrane 5-Endothelium.¹⁴

The cornea consists of the 50 μm thick epithelium, the 450-500 μm thick stroma and the endothelium. The epithelium and the stroma are divided by the epithelial basement membrane (BM) and the 8-10 μm thick Bowman's layer posterior to the BM. Furthermore, between the stroma and the endothelium is the Descemet's membrane. On average, the cornea is thinner centrally (500-550 μm) than peripherally (600-700 μm).¹⁵

Epithelium

The outermost layer of the cornea is the epithelium, which is 5-7 cells thick and measures approximately 50 μm .¹⁷ The epithelium thickens in the periphery and is continuous with the conjunctival epithelium at the limbus. The surface layer of corneal epithelium consists of 2-3 layers of non-keratinized squamous cells. Many cell membrane projections are located on the apical surface of the outermost cells and increase the surface area. The fingerlike projections are microvilli, and the ridge like projections are microplicae. Tight junctions (zonula occludens) join the surface cells along their lateral walls, near the apical surface providing a barrier to intercellular movement of substances from the tear layer and preventing the uptake of excess fluid from the tear film. Additional

adhesion between the cells is provided by numerous desmosomes. The middle layer of the corneal epithelium is made up of two to three layers of wing cells. These cells have wing-like lateral processes, are polyhedral, and have convex anterior surfaces and concave posterior surfaces that fit over cells located posteriorly and the basal cells.¹⁸

The innermost layer is formed of a single layer of columnar basal epithelial cells. These basal cells are approximately 20 μm tall and show a limited division capacity compared to the suprabasal cells which are post-mitotic. Basal cells serve as the source for differentiation into wing and superficial cells. Anchorage of the epithelium to the basal lamina occurs via a large number of unevenly distributed hemidesmosomes. This results in a strong adhesion of the epithelium to the underlying surface.¹⁹

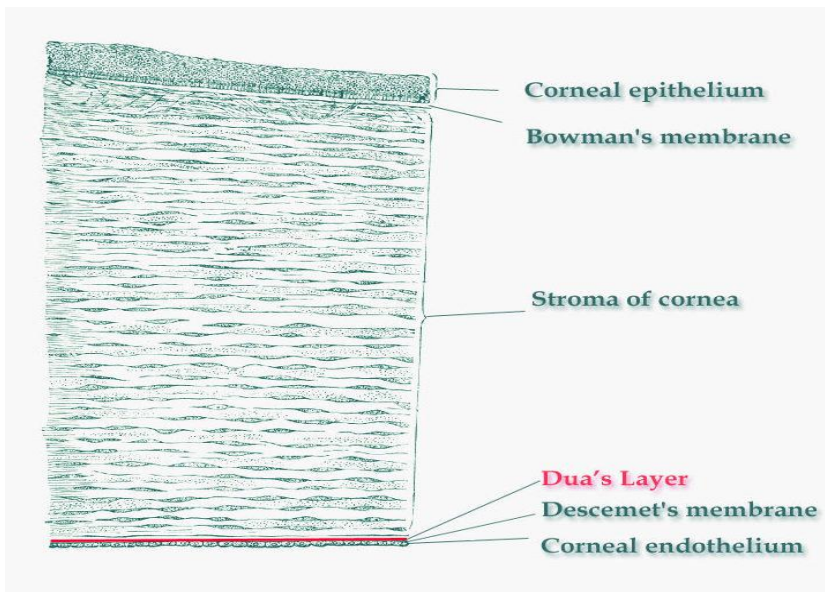


Figure 1. A diagram representing the layers of the human cornea showing the anatomical sight of the newly discovered Dua's layer.¹⁶