Biovance®·3L

HUMAN AMNIOTIC MEMBRANE ALLOGRAFT

OCULAR

Biovance 3L (DDHAM) vs Dehydrated Human Amnion single layer (DHAM) and a single layer Cryopreserved Human Amniotic Membrane (CHAM)

Background: The removal of cellular components, DNA, growth factors, and cytokines, as well as the retention of an intact innate collagen framework with essential extracellular matrix molecules in Biovance 3L Ocular, results in a native three-dimensional scaffold with biocompatibility and the ability to support ocular cell functions, as compared with conventionally preserved amniotic membrane-based products containing residual cells, cell debris, DNA, growth factors and cytokines.

Description: The following compilation of in vitro data presents findings demonstrating how Biovance 3L, DHAM, and CHAM differently affect and interact with the major cell types involved in healing disorders of the eye.

INDICATIONS FOR USE

BIOVANCE•3L Ocular is an allograft intended for use as a biological membrane covering that provides the extracellular matrix while supporting the repair of damaged tissue. As a barrier membrane, BIOVANCE•3L Ocular is intended to protect the underlying tissue and preserve tissue plane boundaries with minimized adhesion or fibrotic scarring. Applications include, but are not limited to, corneal and conjunctival related injuries or defects such as corneal epithelial defects, pterygium repair, fornix reconstruction, and other procedures.

CONTRAINDICATIONS, WARNINGS, AND PRECAUTIONS

BIOVANCE•3L Ocular is contraindicated in patients with a known hyper-sensitivity to BIOVANCE•3L Ocular.

If a patient has an adverse reaction related to the use of BIOVANCE•3L Ocular, immediately discontinue its use. BIOVANCE•3L Ocular should not be used on clinically infected wounds.

The pouch contents are sterile if the pouch is unopened and undamaged. Do not use if package seal is broken. Discard material if mishandling has caused possible damage or contamination. Do not resterilize.

BIOVANCE•3L Ocular must be used prior to the expiration date on the product pouch. BIOVANCE•3L Ocular should not be used together with a collagenase product on the wound. For adverse reaction reporting, telephone 1-844-963-2273.

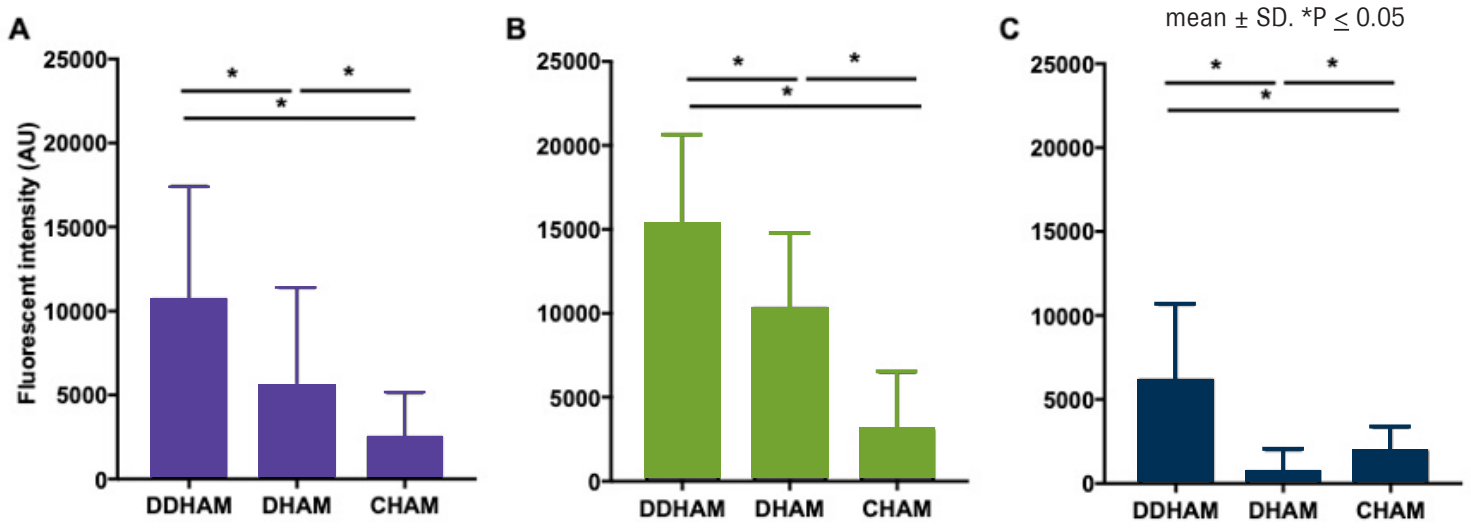
Ocular Healing: Healing of the eye from trauma, disease or surgery to the ocular surface is important. Healthy and orderly progression of wound healing stages is key to achieving the desired outcome.

Healthy and orderly progression may be improved with*:

- Proper ocular epithelial cell viability
- Greater epithelial cell adhesion
- Improved epithelial cell proliferation

* Reference: British Journal of Ophthalmology 1994; 78: 401-408

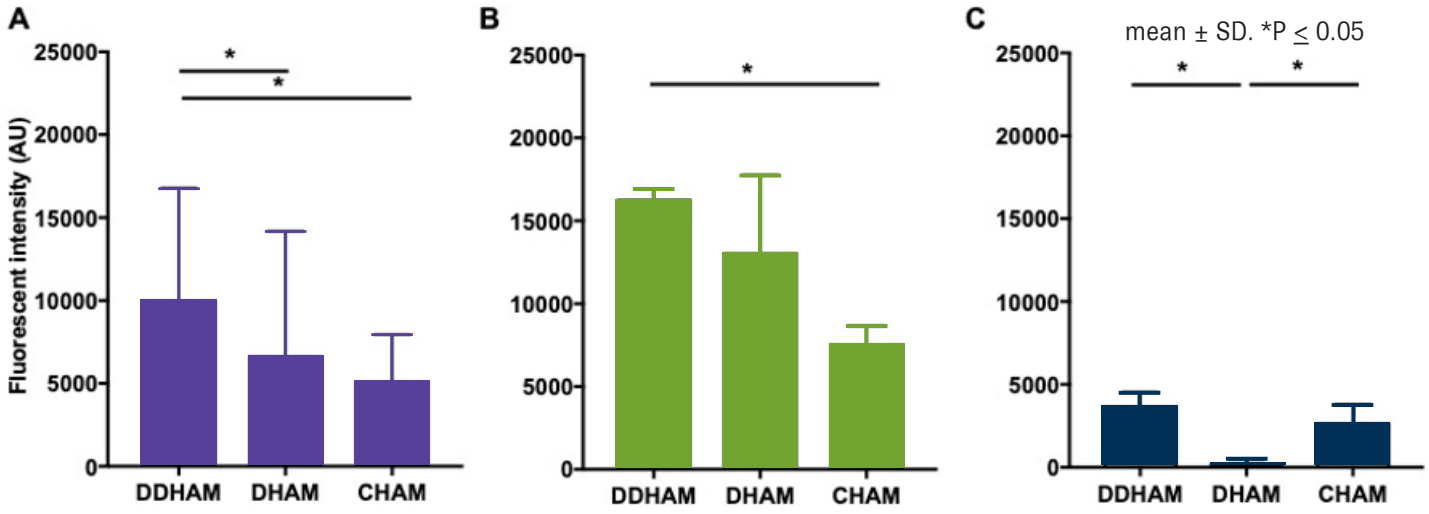
Epithelial Cell Viability by Cell Type and Scaffold



Human corneal epithelial cells and human conjunctival epithelial cells (A), human corneal epithelial cells (B), and human conjunctival epithelial cells (C). The viability of adhered cells was detected using the alamarBlue assay.

In terms of cell viability, DDHAM (Biovance® 3L Ocular) may provide a more suitable scaffold for epithelial cells than CHAM or DHAM.

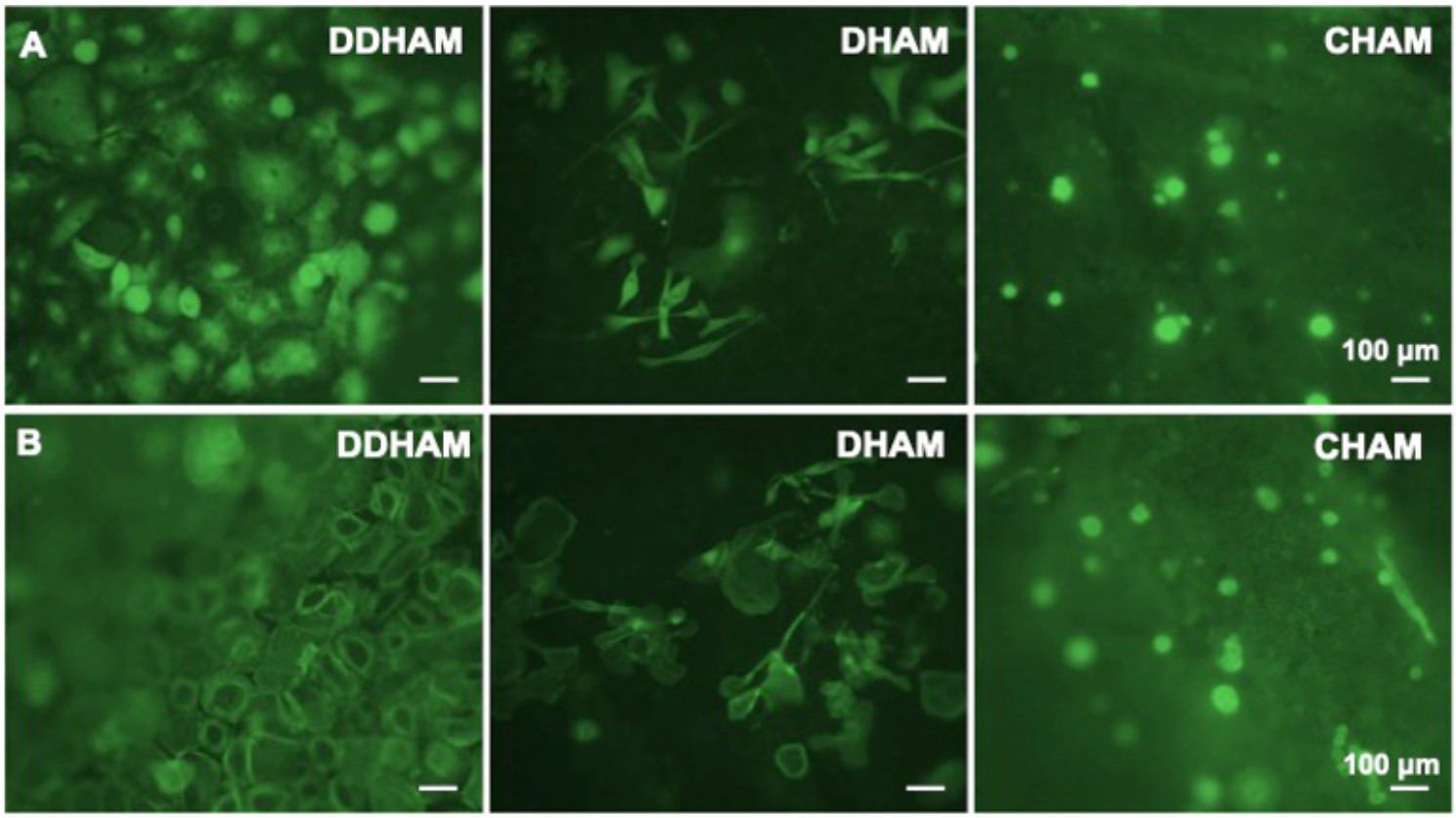
Adhesion of Epithelial Cells on Different Scaffolds



Human corneal epithelial cells and human conjunctival epithelial cells were seeded onto scaffolds and incubated for 24H. Adhesion of human corneal epithelial cells and Human conjunctival epithelial cells (A), Human corneal epithelial cells (B), and Human conjunctival epithelial cells (C).

Human ocular epithelial cell adhesion was significantly greater ($P \leq 0.05$) on DDHAM compared with CHAM and DHAM.

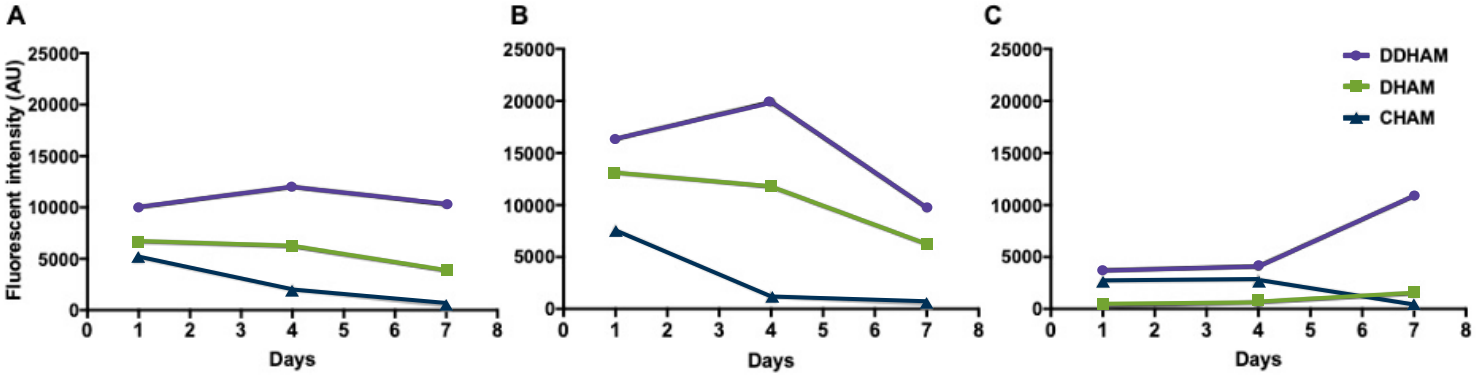
Staining (Calcein AM) of HCEC on Scaffolds at Day 4



Human corneal epithelial cells were seeded on the different scaffolds, cultured, and stained with Calcein AM to visualize viable cells at Day 4 (A).

The morphology of Human corneal epithelial cells on scaffolds was monitored by actin staining on Day 4 (B).

Proliferation of Epithelial Cells by Scaffold



Proliferation of human corneal epithelial cells and human conjunctival epithelial cells (A), human corneal epithelial cells (B), and human conjunctival epithelial cells (C)

Benchtop Study Findings*:

- Human ocular epithelial cell viability was **significantly greater** ($P < 0.001$) on DDHAM (Biovance® 3L Ocular) than CHAM and DHAM.
- Human ocular epithelial cell adhesion was **significantly greater** ($P \leq 0.011$) on DDHAM compared with CHAM and DHAM.
- Human ocular epithelial cell proliferation rate was **significantly greater** ($P \leq 0.011$) on DDHAM than CHAM.
- In terms of cell viability, DDHAM (Biovance® 3L Ocular) may provide a **more suitable scaffold** for epithelial cells than CHAM or DHAM.
- Cell migration was similar between scaffolds and significantly greater than the medium control ($P < 0.001$); HConEpiC migration proved significantly greater than HCEC migration ($P < 0.001$).

* Data on file.

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Please refer to the BIOVANCE•3L Package Insert for complete product information.

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