

# Rebuilding Vision: Evaluating Biomaterials for Next-Generation Artificial Corneas

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**ABSTRACT:** Corneal blindness is a health problem that affects around 10 million people worldwide, but only a fraction of patients receive a corneal transplant due to the lack of donor tissue. To combat this issue, artificial corneas are being developed and tested; however, their success depends heavily on the materials used. This literature review evaluates silk-based polymers, hydrogels, and decellularized corneal tissue for use in artificial corneas, focusing on optical transparency, structural integrity, and host tissue integration. Information was gathered from a wide range of sources, including peer-reviewed studies, clinical trials, and industry reports published since 2016. Findings show that decellularized tissues closely resemble natural corneal structure but face sourcing and immune risks. Hydrogels have good flexibility and transparency but often lack long-term strength. Nanomaterials allow for detailed control of surface and structural features but still require long-term safety assessments. Silk-based and hybrid materials show a balanced performance across the criteria considered, as they offer high strength and low immunogenicity. In the future, specific comparisons between each material and long-term clinical trials are recommended to find the most promising solutions for artificial corneas. These findings support hybrid biomaterial strategies as a practical path toward reducing global dependence on donor corneas.

**KEYWORDS:** Biomaterials, Nanomaterials, Artificial Corneas, Corneal Blindness, Bioengineered Solutions.

## ■ Introduction

Over 10 million people worldwide suffer from corneal blindness. The cornea is the transparent, outermost layer of the eye. It focuses light and protects the inner eye from dust, germs, and injury. The cornea consists of five distinct layers that collectively maintain its strength and transparency. Corneal blindness occurs when this layer becomes cloudy or damaged, which can then block incoming light and cause vision loss.<sup>1</sup>

Despite the effectiveness of corneal transplantation, most patients with corneal blindness never receive treatment due to the global shortage of donor corneas. Limited tissue availability, high costs, and surgical barriers further restrict access to transplantation, particularly in low-resource regions. These limitations underscore the need for artificial corneas as scalable alternatives to donor tissue.<sup>2</sup>

Several biomaterials are being studied for their application in artificial corneas, including silk-based polymers, hydrogels, and decellularized corneal tissues. To function successfully, each material must satisfy three key criteria: optical transparency, structural integrity, and host tissue integration.<sup>2</sup> It is found that Silk offers strength and a low immune response.<sup>1,3</sup> Hydrogels provide flexibility and transparency but break down over time.<sup>4</sup> Decellularized tissues closely match natural corneas but bring some immune concerns.<sup>5,6</sup>

This paper revolves around one question: Which biomaterials offer the most effective combination of transparency, strength, and biocompatibility for artificial corneas? The goal is to inform material selection for future designs and help reduce global reliance on human donor corneas.

## ■ Methodology

The objective of this study was to compare and evaluate three biomaterials that can be used for artificial corneas. The research compared each material in three categories: optical transparency, structural integrity, and biocompatibility/integration. The study aimed to collect information that would help show strengths and limitations regarding the materials for the different categories.

A literature review was conducted to compare and evaluate the three different biomaterials: silk-based polymers, hydrogels, and decellularized corneal tissues. The analysis of each of these materials focused on their optical transparency, structural integrity, and biocompatibility/integration with host tissue. A wide variety of sources, including peer-reviewed studies, systematic reviews, and clinical trials published between 2016 and 2025, were used in the research process. Sources were collected using databases like PubMed, ScienceDirect, Google Scholar, and other informational journal websites. Only articles and publications in the English language were considered for use. Search terms like “artificial cornea,” “corneal scaffold,” “silk fibroin,” “hydrogel cornea,” “decellularized corneal tissue,” and “nanomaterials for corneal regeneration” were used to find relevant information. All studies were synthesized using a qualitative comparative approach to identify relative strengths and limitations across the three biomaterials. Attention was given to emerging material modifications and composite strategies to provide context for current performance and future artificial cornea development. Studies evaluating corneal biomaterials for ophthalmic use were prioritized, and human clinical data trials were preferred over animal ones. Optical transparency was measured through light transmissibility and

whether or not haze/fogginess occurred after placement of the implant. Structural integrity was assessed by comparing the tensile strength of the material to that of native human corneal tissue and whether or not elastic properties were comparable. Biocompatibility and integration were evaluated on the basis of immune responses, nerve regrowth, and long-term implant stability in the living body.

Across the reviewed literature, many strengths and weaknesses of the materials were highlighted. Silk showed good structural integrity but low immune responses. Hydrogels showed promising optical transparency, but lacked a bit in strength without modifications. Decellularized corneal tissues resemble the native cornea really well, but may take longer to facilitate nerve regrowth. A comparison of the advantages and disadvantages of silk-based polymers, hydrogels, and decellularized corneal tissues is presented in Table 1.

### ■ Silk-Based Polymers in Artificial Corneas

Silk fibroin, a protein taken from *Bombyx mori* silkworms and certain non-mulberry species, has become one of the most promising materials for artificial cornea design. This material exhibits favorable characteristics, including optical clarity, high tensile strength, adaptive mechanical properties, and low immunogenicity.<sup>1,3</sup> Silk can be processed into transparent films, membranes, or layered scaffolds that can closely resemble the precisely arranged layers of collagen fibrils that form the bulk of the cornea's middle layer. These arrangements are crucial for the cornea's primary function, which is transparency. Beyond its compositional properties, silk fibroin has been extensively evaluated as a corneal scaffold due to its ability to balance optical clarity with mechanical robustness, making it a strong candidate for artificial cornea applications.

#### *Optical Transparency:*

From an optical perspective, silk-based scaffolds perform favorably when compared to native corneal tissue under controlled fabrication conditions. When processed into ultra-thin films, silk fibroin can achieve light transmission comparable to that of a healthy human cornea. Silk fibroin films transmit a high percentage of visible light – e.g., a 30  $\mu\text{m}$  film of *Antheraea mylitta* (non-mulberry) silk showed about 94.4% light transmittance (400–700 nm), comparable to the native cornea.<sup>1</sup> Such silk films have a refractive index (~1.38–1.44) similar to corneal tissue, enabling minimal optical distortion.<sup>7</sup> Notably, silk's transparency is maintained across various fabrication methods – films cast from different solvents and annealed under different conditions all retained >90% transmission in the visible range.<sup>8</sup> One challenge is that transparency can decrease as the scaffold thickness increases. Thicker silk constructs may scatter light due to  $\beta$ -sheet crystallites or micropores. Recent silk processing techniques (e.g., ethanol annealing or centrifugal casting) allow tuning of optical and mechanical properties without sacrificing clarity.<sup>2</sup> Although few transparency-related weaknesses have been noted, slight reductions in transmittance can occur under certain conditions. For instance, in hydrated hydrogels or hybrid films, the light transmission, while high, may drop to around 85% as seen in one silk/gelatin film study.<sup>9</sup>

Unmodified silk hydrogels may lose some transparency over time, but blending with other polymers or applying chemical modifications can slow or prevent this change. Overall, silk-based polymers can meet the cornea's stringent transparency requirements when engineered at appropriate thickness and microstructure.

#### *Structural Integrity*

A reason silk is popular in corneal applications is because of its mechanical performance. Silk scaffolds can exceed the strength of most natural corneal substitutes. While native cornea tensile strength averages 3–4 MPa, silk scaffolds can equal or exceed these values. For example, multilayer silk film laminates have reported tensile strengths on the order of 10–30 MPa, far above native tissue.<sup>1,2</sup> Additionally, aligned 60:40 (silk: PCL) fibers showed significantly improved ultimate tensile strength and Young's modulus within the acceptable range for corneas.<sup>10</sup> In other words, by adding silk fibroin and aligning fibers, the scaffold's strength and stiffness became similar to native stromal tissue. Processing adjustments—such as glycerol annealing, crosslinking, or combining silk with poly (lactide-co-caprolactone)—allow tuning of stiffness and elasticity; some composites reach 9.3 MPa while maintaining flexibility.<sup>2</sup> One study showed that films cast in formic acid had higher ultimate tensile strength but also lower swelling (more rigidity) than aqueous-cast films, illustrating the trade-off between strength and flexibility that can be engineered.<sup>8</sup> While overly crystalline silk may become brittle, optimized formulations balance rigidity for surgical handling with sufficient elasticity to withstand physiological strain.<sup>3,11</sup> It is also important to note that thicker silk implants can diminish nutrient diffusion.<sup>12</sup> That said, it is essential to consider the trade-off between making silk scaffolds thin enough for transparency and strong enough for mechanical handling.

#### *Biocompatibility and Integration:*

Silk is generally regarded as a biocompatible and low-immunogenic material in ocular applications. Silk fibroin has a long history in sutures and is generally non-inflammatory.<sup>13</sup> *In vivo* implantation studies have shown excellent integration of silk corneal implants. No significant immune rejection or inflammation was observed when silk films were embedded in rabbit corneas.<sup>1</sup> Specifically, no neovascularization was reported in or around a silk fibroin film placed intrastromally for several weeks; the corneal surface remained smooth and clear.<sup>1</sup> Silk can also be chemically modified (e.g., with RGD peptides or methacrylation) to promote cell adhesion and integration further.<sup>11</sup> Silk from non-mulberry silkworms (which naturally contains RGD cell-binding sequences) promoted better cell adhesion than *Bombyx mori* silk: the non-mulberry silk films had significantly higher endothelial cell attachment and more robust focal adhesions, enabling an intact cell layer to form.<sup>14</sup> For corneal stromal cells, composite silk scaffolds have also performed well: a silk nanofibril/GelMA film supported vigorous stromal cell growth, with ~97% of the film area covered by cells after 5 days (versus only ~12% coverage on a pure silk-only film).<sup>9</sup> But there can be limitations to silk-based biomaterials when

it comes to corneal applications. A biological limitation of silk fibroin is its surface chemistry – SF lacks natural cell-binding motifs that many ECM proteins have. Corneal cells (epithelial, stromal, endothelial) can attach and grow on silk. Still, typically this requires the presence of serum or coating the silk with extracellular matrix proteins (like collagen, fibronectin, or vitronectin) to facilitate adhesion.<sup>15</sup> Additionally, native silk fibroin lacks the abundant cell-binding domains found in the extracellular matrix, so that unmodified silk can have lower cell affinity.<sup>14</sup> Overall, silk-based polymers demonstrate excellent biocompatibility, integrating with corneal tissue with minimal immune response. This makes silk a promising base material or component in artificial cornea composites. The main limitation is the need to maintain transparency in thicker formats. Overall, silk-based polymers demonstrate strong mechanical performance and high transparency, though maintaining clarity in thicker constructs remains a key design constraint.

## ■ Hydrogels

“Hydrogels” encompass a broad class of water-swollen polymer networks used for corneal implants. Many hydrogels have optical and biochemical similarity to the corneal extracellular matrix, which is ~78% water and composed of collagen and glycosaminoglycans.<sup>16</sup> Hydrogels are known for high transparency and permeability, but often face challenges in long-term mechanical stability. Advanced chemical crosslinking and composite strategies have improved their performance. In the context of artificial corneas, hydrogels are evaluated not only for their biomimetic composition but also for their long-term optical stability, mechanical durability, and capacity for tissue integration.

### *Optical Transparency:*

Hydrogels can achieve optical clarity comparable to the native cornea, due to their high water content and homogeneous polymer network. A notable example is the bioengineered porcine collagen hydrogel implant (BPCDX, 280–440 μm), which demonstrated light transmission nearly identical to that of a healthy human cornea across the visible spectrum.<sup>16</sup> A 20-patient clinical study with the BPCDX hydrogel implant, all operated corneas maintained clear transparency (graded 4+ clarity) post-operatively.<sup>16</sup> Only a transient mild haze occurred in a few cases during early wound healing, which resolved by 1 week.<sup>16</sup> Another semi-synthetic hydrogel, *Kuragel*, composed of photocrosslinked gelatin and hyaluronic acid, displayed visible light transparency equivalent to a human cornea *in vitro* (above 94% transmission) while restoring corneal clarity in animal models (no scarring or vascularization noted).<sup>17</sup> Importantly, *in vivo* and clinical results affirm that transparent hydrogels can restore corneal clarity. In a rabbit model of corneal injury, a decellularized human-corneal ECM hydrogel prevented scar formation and opacification – treated corneas remained *indistinguishable from healthy corneas* on observation.<sup>18</sup> As for other clinical results, A cell-free recombinant collagen implant in 10 patients maintained full transparency in all implants over 4 years post-surgery.<sup>19</sup> However, earlier generation biosynthetic corneas (e.g., recombinant human

collagen gels) sometimes experienced postoperative haze or thinning, but newer double-crosslinked hydrogels have largely overcome this.<sup>16</sup> Thus, optical performance is a major strength of hydrogels. The challenge is ensuring they remain clear over time (no degradation or cell overgrowth causing haze) and under physiological conditions.

### *Structural Integrity:*

Despite their favorable biological properties, mechanical performance remains the primary limitation when hydrogels are assessed for corneal implantation. Historically, a drawback of hydrogels has been their lower mechanical strength relative to the native cornea, especially when highly hydrated. Many standard hydrogels (e.g., unmodified collagen or gelatin gels) have tensile strengths <0.5 MPa, well below the native cornea's tensile strength of ~3–4 MPa.<sup>2</sup> For instance, a low-solids collagen gel (~0.8% w/v) exhibited an extremely low Young's modulus ~26–27 Pa.<sup>20</sup> Even at higher concentration (4% collagen), the modulus only reached ~243 Pa.<sup>20</sup> Recent reinforcement strategies have been highly effective in addressing this issue. One approach is chemical crosslinking of the polymer network. Collagen-based hydrogels can be crosslinked with agents like glutaraldehyde or genipin, UV-induced polymerization, or enzymatically (e.g., with transglutaminase), which increases network density and stiffness.<sup>19</sup> Another strategy is forming interpenetrating networks or composites. Incorporating a second polymer network (synthetic or biopolymer) can dramatically toughen the hydrogel. Embedding a thin electrospun polycaprolactone (PCL) mesh into a Gel-MA hydrogel increased tensile strength from ~0.1–0.5 MPa to ~3.5 MPa.<sup>21</sup> Similarly, blending collagen with synthetic polymers such as MPC doubled stiffness from 0.6 MPa to 2.1 MPa.<sup>2</sup> These modifications enable hydrogel scaffolds to withstand suturing and even minimally invasive implantation without tearing.<sup>22</sup>

### *Biocompatibility and Integration:*

Hydrogels for corneal use are engineered to be biocompatible, supporting cell viability and integration with host tissue while minimizing immune rejection.<sup>4</sup> Zhao *et al.* observed over 95% viability of human corneal epithelial and stromal cells cultured on their HCSP scaffold, indicating no cytotoxic leachates. In a landmark Phase I clinical trial, a biosynthetic cornea made of crosslinked recombinant human collagen (RHCIII) was implanted in 10 patients with corneal blindness.<sup>19</sup> The outcomes demonstrated excellent biocompatibility: the cell-free collagen implants became stably integrated into the patients' own corneal stroma, with complete re-epithelialization over the implant and even nerve regeneration into the graft.<sup>19</sup> Another study introduced *Kuragel*, a gelatin/HA-based hydrogel, into rabbit corneal injuries affecting both epithelium and stroma. *Kuragel* was formulated for tissue adhesiveness and minimal swelling, allowing it to be applied as a sutureless filler in the defect. The *in vivo* results were notable: the hydrogel encouraged full re-epithelialization within 4 weeks, and within 3 months, the corneal stroma had regenerated with organized collagen and a restored sub-basal nerve plexus present.<sup>17</sup> Also, in a rabbit

model of lamellar keratoplasty, the HCSP implants supported rapid re-epithelialization without sutures. They avoided the typical foreign-body complications – no significant haze, neovascularization, or graft rejection were observed.<sup>4</sup> However, long-term implant stability remains a consideration, and recent data are helping identify which designs perform best. For instance, a “LiQD” peptide–PEG hydrogel, designed as a fully synthetic corneal substitute, supported tissue regeneration in a pig study but developed some post-operative haze and neovascularization in all implanted eyes within 1 year. The transient haziness was attributed to the material’s swelling and bioresorption profile, highlighting the need for balanced degradation rates. Nonetheless, even in those cases, there were no severe rejections – the immune response was manageable, and corneas achieved functional thickness and barrier function.<sup>19</sup> Overall, studies show that hydrogel corneal substitutes can biologically integrate with host tissue: they support epithelial coverage and nerve ingrowth, and remain stable long-term *in vivo*.<sup>4,23</sup> This favorable biocompatibility profile is critical, as it translates to improved healing, transparency maintenance, and implant longevity in artificial cornea applications. Collectively, hydrogels offer excellent optical clarity and biocompatibility, but long-term mechanical stability depends on reinforcement strategies.

### ■ Decellularized Corneal Tissue

Decellularized corneal tissue involves using a natural corneal extracellular matrix (ECM) – usually sourced from donated human corneas or animal corneas (e.g., porcine or bovine) – and removing all cellular components to mitigate immune rejection. A good approach aims to leverage the biomimicry of a real cornea’s structure and chemistry, while eliminating donor cells that would cause rejection. When assessed as artificial corneal substitutes, decellularized tissues are primarily evaluated based on how effectively they preserve native corneal structure while minimizing immune rejection and supporting long-term integration.

#### **Optical Transparency:**

Decellularized corneal tissues can achieve high optical clarity, approaching that of the native cornea, provided swelling is controlled and tissue architecture is preserved. A 2024 study using high-hydrostatic pressure decellularization produced “transparent” acellular porcine corneas with ~86% light transmittance (380–770 nm average), comparable to fresh human corneas (~87%).<sup>5</sup> In rabbit implants, these grafts were essentially clear and indistinguishable from surrounding tissue within days post-surgery, indicating excellent restoration of transparency *in vivo*.<sup>5</sup> Similarly, a decellularized human corneal scaffold (deoxycholate/DNAse method with dextran) showed no significant loss in optical transmission versus native cornea.<sup>24</sup> But swelling and dehydration can affect performance in clarity. If osmotic measures are not used during decellularization, the corneal stroma tends to swell and become hazy. For example, decellularization without dextran led to a ~10–15% drop in transparency.<sup>24</sup> However, dehydration treatments can reverse this: simply incubating the decellularized tissue in

glycerol or dextran solution rapidly restores transparency by collapsing excess fluid.<sup>6,24</sup> Overall, decellularized corneal tissue, being derived from a transparent tissue, can provide optical performance essentially on par with a donor cornea.

#### **Structural Integrity:**

Mechanical strength and elasticity of decellularized corneal scaffolds are critical for long-term durability. Research in the past six years indicates that while decellularization can alter corneal micro-architecture, proper processing (and optional crosslinking) yields scaffolds with robust mechanical properties comparable to donor tissue. To further improve strength and prevent any post-implant thinning or bulging, researchers have applied collagen crosslinking treatments to decellularized corneas. This can dramatically increase stiffness and resistance to deformation. A notable example is a proprietary 4-step processing of porcine corneal lenticules (including decellularization, enzymatic wash, tissue compression, and chemical crosslinking) developed for keratoconus treatment.<sup>25</sup> The result was a thin (~90  $\mu\text{m}$ ) implant with a Young’s modulus ~25 MPa – roughly 127% stiffer than the native cornea (unprocessed porcine stroma ~11 MPa).<sup>25</sup> Another study created a chemically cross-linked decellularized pig cornea (using EDC/NHS and  $\gamma$ -irradiation) and found its ultimate tensile strength and resistance to enzymatic digestion were significantly improved over native tissue.<sup>26</sup> Importantly, the transparency of these crosslinked grafts remained similar to that of untreated corneas.<sup>26</sup> Decellularized corneal scaffolds have also proven durable in both laboratory and surgical settings. For instance, acellular porcine grafts implanted in patients for more than 2 years showed no thinning; the grafts maintained their shape and thickness, similar to a normal cornea.<sup>27</sup> In a rabbit infection model, a cross-linked decellularized cornea withstood the proteolytic/inflammatory environment, preventing corneal perforation better than standard treatments.<sup>26</sup> Flexibility of the scaffold is also crucial for conformance to the ocular surface. High-pressure decellularized corneas, for example, had a refractive index of ~1.367 (vs 1.373 native) and normal hydration, indicating the stromal structure was intact enough to preserve biomechanical and optical function.<sup>5</sup> Surgeons in clinical trials noted that acellular grafts could be sutured similarly to donor tissue, facilitating standard keratoplasty techniques.<sup>6</sup> If anything, decellularized corneas are sometimes softer or easier to cut due to the absence of cells, but overall, handling characteristics are very close to a live cornea.

#### **Biocompatibility and Integration:**

Biological integration represents the defining advantage of decellularized corneal scaffolds, but it also introduces variability in healing outcomes. A decellularized corneal implant must integrate with the host tissue, supporting cell repopulation, normal wound healing, and nerve regeneration while avoiding immune rejection. Recent studies provide encouraging evidence that decellularized corneas are biocompatible and integrate well *in vivo*, though complete integration (especially neural) can be gradual. Clinical xenotransplantation trials in China implanted acellular porcine corneas in patients with

corneal ulcers and keratitis. After 2 years, 22 of 23 grafts remained clear and in place with no rejection episodes reported.<sup>6</sup> Only mild, transient postoperative inflammation was noted, manageable with standard steroids. Another cohort of 37 patients received decellularized porcine grafts for fungal keratitis and showed 100% retention at 3 years without immune rejection or significant complications.<sup>6</sup> Functional integration also requires that corneal nerves regrow into the graft to restore sensation and neurotrophic support, and this can be a long process. Clinical experience with human corneal transplants shows that stromal nerves begin to penetrate a graft by ~2–3 months post-op, but the superficial nerve plexus in the epithelium often takes 1–2 years to return fully, and normal corneal sensitivity may require ~3 years to recover. In decellularized porcine grafts, nerve trunks have been observed regrowing into the transplant during long-term follow-up (e.g., a 12-month dog study). The dog study also noted improved corneal nerve re-innervation in the decellularized scaffold that had been pre-populated with human cells, compared to a cell-free scaffold. This suggests that promoting a biologically active environment in the graft can influence nerve return. Furthermore, decellularized corneas generally induce a milder healing response than full-thickness grafts. Some studies note a delay in complete healing with decellularized grafts: for instance, initial corneal haze can persist for several months post-implant until remodeling resolves it. Over longer periods, however, remodeling tends to restore a more normal matrix structure. In clinical observations, patients with decellularized cornea grafts experienced gradual clearing over a year or more.<sup>27</sup> In summary, decellularized corneal scaffolds closely replicate native tissue properties, though slower nerve regeneration and processing variability limit immediate clinical adoption.

**Table 1:** Advantages and Disadvantages of Artificial Corneal Biomaterials.

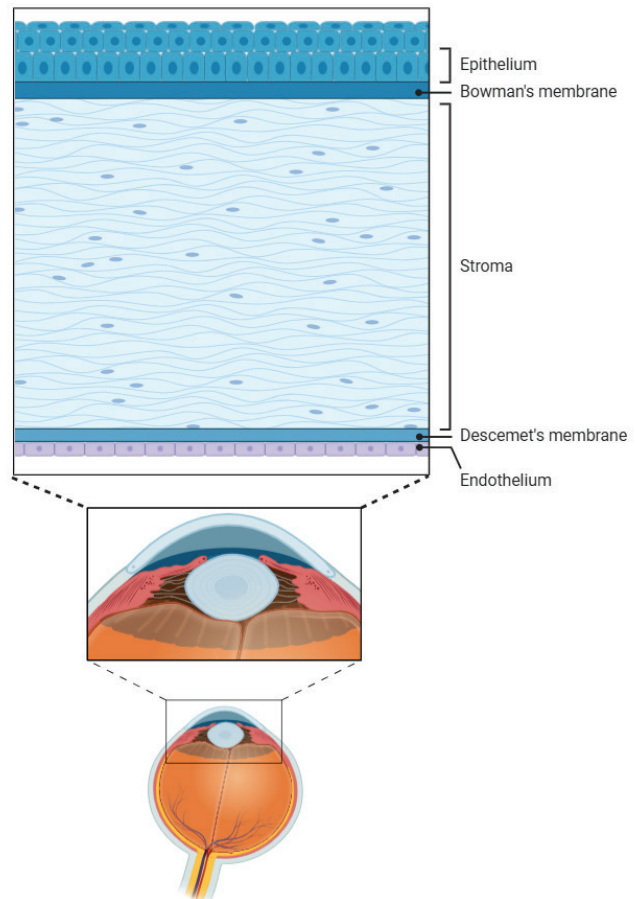
Material	Advantages	Disadvantages	References
Silk-based Polymers	<ul style="list-style-type: none"> <li>High optical clarity- 94.4% light transmittance (400–700 nm)</li> <li>Tunable with various processing styles</li> <li>High tensile strength depending on the formulation technique</li> </ul>	<ul style="list-style-type: none"> <li>Optical clarity can decrease with thicker scaffolds</li> <li>Risk of brittleness if overly crystalline.</li> <li>Variable degradation rates <i>in vivo</i>.</li> </ul>	<p>Hazra <i>et al.</i> <sup>1</sup></p> <p>Formisano <i>et al.</i> <sup>2</sup></p> <p>Jameson <i>et al.</i> <sup>11</sup></p> <p>Manoochehrabadi <i>et al.</i> <sup>3</sup></p>
Hydrogels	<ul style="list-style-type: none"> <li>High optical transparency (similar to native cornea)</li> <li>Stable implants and improved vision were shown in clinical studies.</li> </ul>	<ul style="list-style-type: none"> <li>Weaker tensile strengths (&lt;0.5 MPa)</li> <li>Long-term stability is currently dependent on reinforcement techniques.</li> </ul>	<p>Kong <i>et al.</i> <sup>21</sup></p> <p>Rafat <i>et al.</i> <sup>16</sup></p> <p>Zhao <i>et al.</i> <sup>4</sup></p>
Decellularized Corneal Tissue	<ul style="list-style-type: none"> <li>Mimics natural corneal transparency: ~86% light transmittance (380–770 nm average).</li> <li>Crosslinking techniques can dramatically increase structural integrity</li> </ul>	<ul style="list-style-type: none"> <li>Swelling and hazing can occur if not properly treated.</li> <li>It can take a long time to heal and facilitate nerve regrowth</li> </ul>	<p>Hashimoto <i>et al.</i> <sup>5</sup></p> <p>Poliseti <i>et al.</i> <sup>24</sup></p> <p>Lin <i>et al.</i> <sup>26</sup></p> <p>Fernández-Pérez <i>et al.</i> <sup>27</sup></p>

Table 1 highlights the strengths and limitations of the three biomaterials compared in this review. Silk-based polymers stand out for their high tensile strength and optical clarity, but they require levels of modification to facilitate their best performance. Hydrogels are excellent when it comes to optical clarity, but can lack in the category of strength, as they require chemical modifications and reinforcement strategies for the best long-term use. Decellularized Corneal tissue most clearly

mimics the native cornea in terms of optical transparency and structural integrity. However, variable processing techniques and slower recovery times for these materials can be a limitation. Overall, these findings show that each material offers its own unique strengths, and it is important to recognize these strengths for future innovation in this field.

## Discussion

Figure 1 illustrates the layered structure of the human cornea, highlighting the anatomical features that artificial cornea biomaterials aim to replicate in terms of transparency and mechanical support.



**Figure 1:** Layers of the Cornea. This figure shows the 5 main layers of the human cornea: the epithelium, Bowman's layer, stroma, Descemet's membrane, and the endothelium. These layers are essential for maintaining the cornea's strength and transparency, which are the same properties evaluated in this study to guide artificial cornea design. Created using BioRender.

The findings across the three biomaterials compared in this review highlight a promising future for the development of artificial corneas, yet challenges remain in the field. Each of the materials compared shows a strength in at least one of the categories used for assessment: optical transparency, structural integrity, and host tissue integration. But, no single method currently meets the capacity for a clinically functional substitute with exceptional performance in all three categories.

Optical transparency is the most consistently achieved property. Silk-based polymers and hydrogels regularly demonstrate light transmittance near that of the native cornea, while decellularized tissues preserve transparency when tissue architecture

is maintained during processing. These findings, along with the analysis of each material in different contexts, demonstrate that transparency is very important for bioengineered corneas, but not a primary component for clinical success. The challenge lies in maintaining corneal clarity in long-term implantation trials, as postoperative haze and other scarring issues can occur in the process.

Structural integrity presents a wide variation of results across the three materials compared. For example, silk-based biomaterials continue to demonstrate tensile strength values that are comparable to those of the native cornea, and sometimes even exceed those values. Hydrogels, while flexible and compatible with outside tissue, can often degrade under physiological conditions. However, they can be reinforced and chemically modified with other polymers to increase robustness. Decellularized corneal tissues can maintain much of the natural strength of the natural cornea, especially when crosslinking techniques are applied. However, mechanical performance can still vary significantly depending on the donor source and other processing methods.

Biocompatibility and Integration represent another decisive factor for current and future clinical outcomes. Silk-based scaffolds are generally supportive of cell adhesion, though nerve regeneration with this biomaterial appears slower than with donor tissue. Hydrogels demonstrate strong compatibility, and clinical trials show minimal immune responses and rejection without the need for significant immunosuppression efforts. Decellularized tissues most closely replicate natural biology by supporting nerve regrowth processes, but they can carry risks of immune reaction responses if residual antigens are not fully removed. Long-term studies also show that decellularized corneal tissues may have initial haze or remodeling that can gradually recover over months to years.

Overall, these results signify that hybrid or compost strategies for corneal biomaterials are an effective path moving forward. Silk's mechanical strength, hydrogel's flexibility and optical clarity, and the biological similarity of decellularized corneal tissues provide promising characteristics for future studies. Combining each material's strength into multi-component scaffolds can help overcome challenges related to single-material composites.

Progress over the last decade points to a promising future for the potential of these materials to meet the urgent need for donor cornea alternatives. Yet, significant challenges continue to remain. Most studies are limited to animal trials or short-term human trials, with limited follow-up measures. Standard ways of testing optical, mechanical, and immunological trends are crucial for further comparison between the materials under examination. Additionally, expanding the duration of human clinical trials will be important for assessing safety and success in long-term applications.

Artificial corneas are an essential innovation to combat the global problem of corneal blindness. Further collaboration between material scientists and clinical ophthalmologists will be helpful to improve the biomaterials and their applications further.

## ■ Conclusion

Artificial corneas will continue to remain a critical area for research due to the fact that corneal blindness and other related issues will affect millions of people worldwide. This literature review compared silk-based polymers, hydrogels, and decellularized corneal tissue against three criteria: optical transparency, structural integrity, and biocompatibility. Each biomaterial proved successful in at least one category that was reviewed, but none showed complete excellence in all three fields. Silk showed strength and stability, hydrogels proved great transparency, and decellularized tissues most clearly exhibited natural corneal structure.

Evidence from studies points toward hybrid biomaterials being able to combine the strengths of multiple other biomaterials. For example, silk's strength, hydrogel's transparency, and decellularized tissues' biological resemblance could form composite scaffolds to address current restrictions.

Artificial corneas continue to become more clinically advanced as research on the topic progresses, but further refinements are still needed to achieve the safest and most functional solution. Continuing research on bioengineered solutions for artificial corneas will continue to be extremely impactful for the millions of people battling corneal blindness.

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