# Biogracompatability of rigid gas permeable care systems

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In order to intimize the clinical success and wearing experience of contac lenses fitters have often requested of reseachers and those involved in developing new products, lens materials and care systems which are more biocompatable. The term biocompatability is used broadly to imply tailored, deposit resistance and freedom from epithelial trauma. Within the biomedical and implatable device field a more generically accepted definition of biocompatability is the ability of a compound or device to perform a function with an appropriate host response in a specific application. In contact lens clinical practice it may be easier for the fitter to understand what constitutes an inappropriate host response rather than the histopathollogy of an appropriate host response.

## Inappropriate host responses

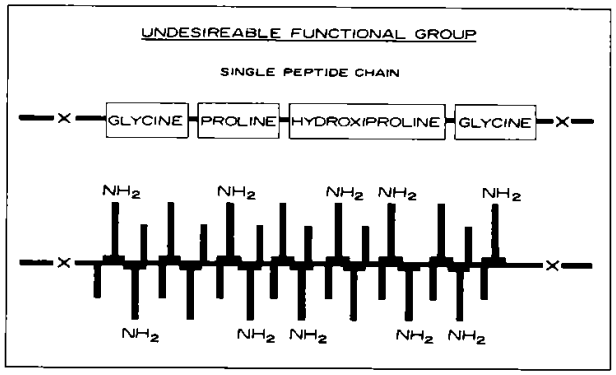
**Acute inflammation:** Acute inflammation is an easily recognized inappropriate host response to contact lens wear. This inflammation maybe characterized by circumcorneal injection and chemois, diffuse bulbar conjuntival hyperenia and chemosis, tarsal conjunctional congestion, or in unusually severe inflammation, episcleral involvement. The acute inflammation may be focal or diffuse depending on the etiology. Acute inflammation is usually or rapid onset and moderate severity.

**Chronic inflammation**: Chronic inflammaton is the second inappropriate host response. This type of inflammation is often the result long-term chemical or mechanical irritation. The onset is slow, as is the resolution even upon cessation of lens wear. Often, the chonic inflammation is mild-to-moderate, allowing the patient to continue lens wear, but not without the dissatisfactions always having «slightly red eyes».

**Fibroplasia:** Fibloplasia is an inappropriate host response characterized by infiltration and proliferation of fibroblasts that create fibroplastic or hyperplastic tissue which may appear as tufts or leashes. This is most commonly seen at 3 or 9 o'clock in the contact lens wearer, where, due to chronic desiccation or mechanical irritation, a fibroplastic mounding of conjunctival tissue can form. In severe cases, the fibroplasia may be accompanied by a vascular leash. All fibroplasia is undesirable, specially if it occurs in the optically transparent cornea where it will compromise optical integrity.

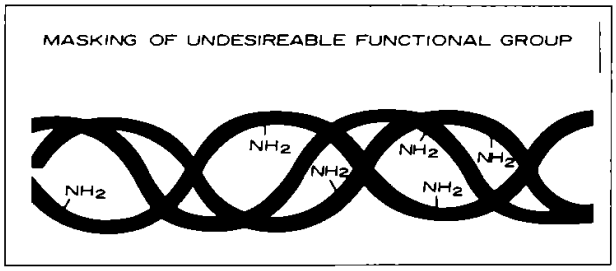
**Autoimmune reactions:** Autoimmune reactions, such as those occurring due to the antigenic or mechanical stimulation of protein deposition in Giant Papillary Conjunctivitis or the reaction to Staphylococcus toxins producing peripheral sterile ulcers are also inappropriate host responses which are undesirable.

Thus, it is the objective of developers of contact lenses and care systems to design them in such a way as to minimize the potential for these inappropriate host responses or avoid them completely by selecting compounds and formulations that enhance biocompatability. To accomplis this requires the understanding that biocompatability is a function of molecular structure. Ideally, we would like to use materials and solutions that have molecular structures thar are: Free of functional groups capable of evoking an undesirable cellular response. Specifically, the amino group found insingle peptide chains which are freely available to contact ocular tissue are capable of evoking such a response.



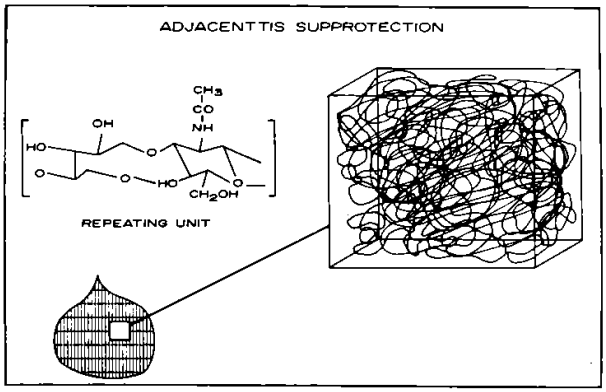

Thus, materials or solutions composed of even very small amounts of components with amino groups «exposed» as in the case of single peptide chains should be avoided.

**Capable of Masking Undesirable Functional Groups:** In the example of collagen, although this compound is composed of sequences of aminoacids and thus has free amino groups. It is a triple helix structure so that the groups are inter-twined and masked from being in contact with tissue.




In this configuration the masking of groups that are undesirable and could evoke and inappropriate chemotactic or autoimmune host response is limited.

Capable of Offering Protection of Adjacent Tissue - An example of a structure capable of offering mechanical protection of adjacent tissue is the glycosaminoglycan backbone of hyaluronic acid. This polysaccharide derivate as well several others exhibit the conformational freedom that allows them to form random molecular coils in solutions. These molecular coils offer spring-like cushioning to adjacent tissue. In addition to a mechanical cushioning, hyaluronic acid, as well as other vicoselastic substances have a good ability to adhere and coat material surfaces. Thus, it is possible to adhere or coat «molecular coils» or material surfaces by utilizing the proper viscoelastic compounds.




For the purposes of this manuscript, we will utilize the concepts of biocompatability outlined above to examine the functional requirements of an RGP Care System and discuss how to optimize the overall contribution that the conditioning solution can make to wearer satisfaction.

## Functional requirements of RGP conditioning solutions

Mechanically cushion the lens-cornea interface - When placing an RGP lens on the eye, in order to en hance the wearer's comfort it is important to design a solution that cushions and mechanically protects the cornea from the presence of the lens. This is specially true in relatively mew and unadapted wearers but is also a noticeable benefit to adapted patients during each lens insertion. Cushioning and mechanical protection are directly related to the polymer properties of viscosity and viscoelasticity. Both properties may be optimized by selecting components of the appropriate molecular structure and molecular

weight. In the laboratory both properties are directly measurable by readily available instruments such as the Cone/Plate Viscometer and the Rheometer. Clinically however, how much viscosity is actually requiered to enhance insertional comfort? To answer this question, some clinical research was performed whereby six different solutions of viscosities, ranging from approximately 1-40 centipoise (cps) were given to patients who were them asked to rate the comfort on an analog scale.

The results indicated that:

- viscosity is a very important solution property

- solutions with low viscosity (less than 5 cps) are significantly less preferred than solutions with somewhat higher (15-40 cps) viscosities.

- optimum preferred viscosity for handling, cushioning , and comfort is 35-40 cps.

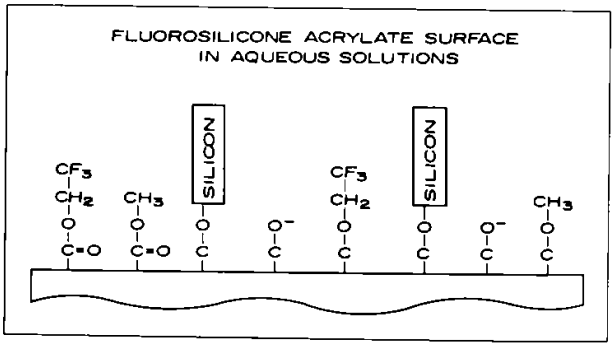
- some additional property, as driven by the type of viscosifier, can further enhance comfort.

It is this additional property that may be useful in addressing the next functional requirement.

**Mechanically Protect the Lens-Lid Interface:** Clinically, we know that a great source of discomfort in wearing RGP lenses may be due to the friction that occurs at the interface of the superior edge fo the lens and the upper lid. It is at this interface that significant shear forces will be applied to the tarsal conjunctiva and potentially be irritating. If we can select polymeric components that protect this interface as well as reduce the friction across this interface, it would be of benefit to the comfort response. In addition , if we could also coat the lens surface with a polymeric solution that lubricated the lens surface, this behavior would also enhance comfort. Thus, to enhance comfort, the polymeric solution, besides being of the appropriate viscosity should be capable of providing viscoelasticity and lubricity to the system.

## Render the lens surface hydrophilic

It is well known that the surfaces of contemporary RGP lenses are composed of a random arragement of functional groups that reflect the inclusion of the various monomers to achieve specific bulk and surface properties. The inclusion of organic acids, such as methacrylic acid, and sulfoethyl methacrylate predispose the surface to undergo electrostatic interaction and hydrogen bonding with solution components. Therefore, the most effective way to render the surface hydrophilic is to include a positively charged hydrophilic component to be attracted to the electrostatic sites and compounds like polyvinyl alcohol that can be attracted to the surface. By achieving both interactions concurrently, the lens surface will easily be coated by a hydrophilic layer.




## Disinfect the lenses

Although RGP lenses are rarely connected to ocular infections, the routine disinfection of worn lenses is an important part of the care regimen, a bacteria may adhere directly to lens surfaces or to deposits on lens surfaces. Thus, the first step in lens disinfection is to thoroughly clean the lens by rubbing with a surfactant cleaner. The rubbing disinfections step can be even more effective if

performed with a combination surfactant abrasive cleaner as this will further enhance the friction applied to the lens surface to remove debris and microorganisms if present. Nonetheless, the conditioning solution must possess sufficient biocidal activity to meet both regulatory, as well as, practical disinfection standars.

## Maintainig contamination - free container

As important, and, perhaps even more important as disinfecting lenses, the conditioning solution should be capable of resisting contamination and rebound growth of microorganisms inadvertently introduced into the bottle.

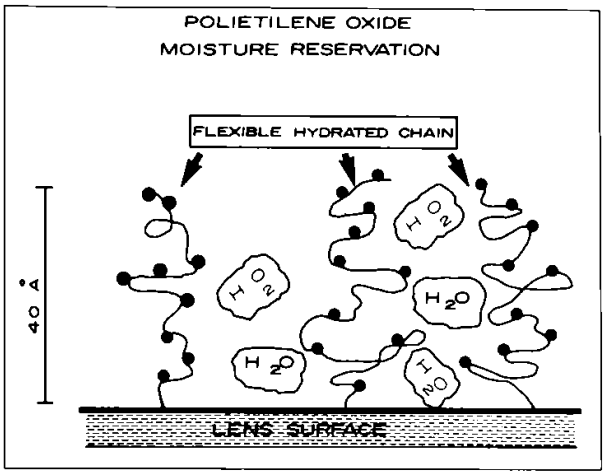
## Render the lens surface biocompatable

Within the biomedical and implantable device fields, a number of biocompatible polymers have been utilized in various applications. These include ollagen and hyaluronic acid, as already mentioned, as well as chondroitan sulfate and polyethhylene oxide. If we examine the properties of polyethylene oxide in depth, a number of surface properties that are potentially beneficial for contact lens and care system applications becomes evident.

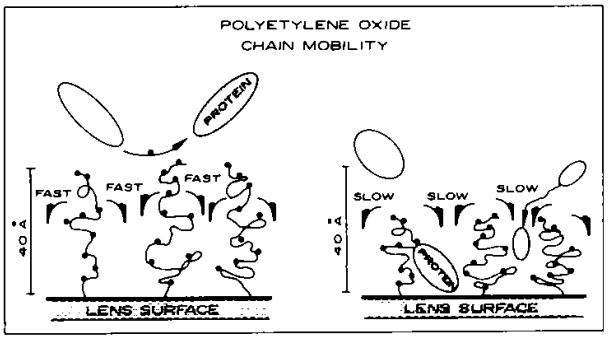
Polyethylene oxide (PEO) has a fairly simple structure that can be represented by the following:

$(CH_2 - CH_2 - O)_n$

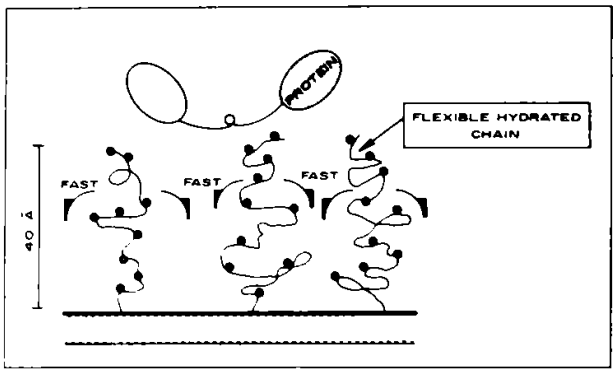
By tailoring the chain length (n=number of units) PEO's have been reported to provide moisture preservation (humectant) characteristic and are actually considered to provide «liquid-like» surfaces due to the hydrophilic nature of the chains.




The «liquid-like» surfaces provides by PEO's or PEO coated surfaces are reported to be responsible for the lubricious or « slick» nature of these surfaces as well. The flexible hydrated PEO chain is in a constant state of mobility. By selecting the optimum chain length we can create a «dynamic surface» through the continuous and rapid movement of the chains. Thus, tear protein are «whisked» away or «beaten» from the lens surface. This chain mobility and resultad «dynamic surface» account for why PEO surfaces are repulsive to protein and are under development for coating on heart valves, vascular shunts, and urinary catheters where deposition of protein would be quite detrimental.




Finally, by arriving at the appropriate chain length and distribution of PEO chains it is possible to create a surface that effectively mimics the epithelial microvilli through the creation of «molecular cilia».




Thus, it is proposed, that the PEO interface is biocompatible because it creates liquid-like surfaces that are dynamic (in a constant state of movement), repulsive to undesired proteins, and capable of mimicking epithelial microvilli for desired protein absorption.

When designing RGP care system components, it would be ideal if the compound could provide both a PEO-like interface and a hyaluronic acid-like protective cushion.

This would «biocompatabilize» the conditioning solution and provide a clinically comfortable wearing experience from insertion through longer term wear.

In summary, for a targeted approach to enchancing wearer comfort, the design of an RGP conditioning solution should include components that are capable of creating an optimum insertional cushion, a hydrophilic and lubricious coating on the lens and a surface capable or repelling protein.