CHAPTER - 5

SELECTION OF OTHER ADDITIVES
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The last few years have seen significant improvements in contact lens solutions. The benchmark for the ideal solution is:

1. A solution that is non toxic to the ocular surfaces.
2. Possess anti-microbial activity to kill bacteria, fungi and \textit{Acanthamoeba}.
3. Contain a preservative so that it continues to disinfect the lens while in prolonged storage.
4. Wets and keeps the lens hydrated so that it is comfortable to insert.
5. Removes protein, lipid, calcium, mucin and other debris.
6. Possess similar pH and tonicity to human tears.
7. Easy to use to aid compliance and easy to store.

Second generation Multi Purpose Solutions (MPS) have inward antimicrobial efficacy. They have surfactants such as Poloxamer and Poloxamine to remove lipids, proteins and debris and contain sequestering agents with a negative charge, to remove protein and calcium on a daily basis such as Citrate, Hydranate\textsuperscript{TM}, Phosphate, Trisbuffer and EDTA. Many now have enhanced buffering systems as well as lubricating agents. Following excipients are incorporated in the multipurpose solutions:

\textbf{Sequestering and Chelating Agents}

These agents are added to enhance the antibacterial effect of the main preservative. They have negatively charged ions which facilitate the removal of calcium and protein from the lens surface.

EDTA is chelating agent which produces its effect by removing calcium ions from solutions and disrupting the cell wall of microorganisms. It is added to most of the multipurpose solutions and works synergistically to enhance disinfection and reduce calcium ions. It is compatible with Polyhexamethylene biguanide (PHMB) and acts
synergistically. EDTA is capable of inactivating metal in a solution and enhancing the
effectiveness of other agents such as Polyquad, Polyhexanide by some active disruption
of the cell wall of microorganisms. Besides being a chelating agent, it prevents
discoloration due to trace metals, prevents oxidation catalized by trace metals and
stabilizes other compounds.

Its effectiveness and lack of toxicity are evidenced by the ubiquitous use of EDTA or one
of its congeners in contact lens solutions.

Disodium edetate and EDTA act as both are chelating agent, stabilizers and cleansing
agents. Disodium edetate is more water soluable hence used in the present research work.
The structure of EDTA is given in Fig. 10.

\[
\begin{align*}
\text{NaOOCCH}_2 & \quad \text{CH}_2 \text{COONa} \\
| & | \\
\text{N} & \text{N} \text{.} \text{2H}_2\text{O} \\
| & | \\
\text{CH}_2 & \text{CH}_2 \\
| & | \\
\text{COOH} & \text{COOH}
\end{align*}
\]

**Fig. 10: Structure of Disodium edetate**

**Viscosity Imparting Agents:**

These are added to control the thickness of the solution. These ingredients may be used as
lubricating and clinging agent. The most common being methyl cellulose. The other
compounds are Polyvinyl Alcohol, Hydroxy propyl methyl cellulose or Hypromellose.
These compounds act as thickener, protective colloid, binders, stabilizers and suspending
agent. Their primary purpose is to cushion the lens against the eye. They do this by
lubricating the lens and providing the surface of the lens with a mechanical buffer for a
short time after insertion. Through this action they also help prevent contamination from
the fingers.
Methyl cellulose is the most common of these agents. It can increase the contact time of drugs on the surface of the eye.

Another attribute of the viscosity building agent is the ability to function as wetting agent. Methyl cellulose and Hydroxy propyl methyl cellulose both have adhesive properties that make the lens appear to be wet when it is removed from the soaking solution.

Methyl cellulose or HPMC can be used as viscosity imparting agent, lubricating and wetting agent. HPMC is selected although it has same properties as Methyl cellulose but it gives clear solution and does not gel on heating. Therefore it is useful in preparations where gel formation is undesirable.

Lubricating Agent

These have been added to some of the new solutions in order to reduce surface tension, improve wetability, increase viscosity and improve contact lens comfort on insertion. HPMC has been chosen to act as lubricating agent because it protects the eye from dryness. It has been used in international brands usually as wetting and lubricating agent.

Surfactants

Nearly all of the new multi purpose solution contain either poloxamer or poloxamine which are surfactants with a high molecular weight and which are non toxic and non ionic. They not only clean the lens of proteinaceous material and solubilize lipids and debris, but may also adhere to the contact lens surface and make it wetable and more comfortable to the patient. With Allergan’s New Complete Pro-Tec, the lubricant Hydroxy propyl methyl cellulose assists lipid cleaning. Hence HPMC + Disodium Edetate + Poloxamer 407 + Polyhexanide are compatible and a unique combination.

Abatron’s Quattro Multifunctional Solution for soft lenses contains lubricant which is a formulation that features high and medium molecular weight non ionic surfactants. Ciba Vision’s Solo Care Soft contains Triklens – a negatively charged surfactant which aid the action of Poloxamer 407. All conventional surfactants even non ionic were not selected due to their less efficient action than Poloxamer 407.

Octaxynol being non ionic, good detergent emulsifier and dispersing agent is ocular toxic and hence rarely used.
Poloxamer 407 is efficient and compatible and hence selected as the surfactant in the present research work.

**Buffering Agents**

They maintain the pH of the solution. Ideally the pH should be close to the tears i.e approximately 7.45 (± 0.2). The buffers Boric acid, Borate, Phosphate/Phosphore and Citrate all enhance the efficacy of Polyhexanide and also increase the ability to remove proteins particularly from group IV FDA type contact lenses. Borates are preferred because apart from buffering action, these have antiseptic action as well.

The solution should therefore be lightly buffered in order to allow the solution to adjust to the pH of the tears as quickly as possible.

**Tonicity Agent**

The tonicity of the solution should be maintained as close to the human tears as possible. Potassium and Sodium both help to maintain the electrolyte balance. Sodium Chloride is used as aqueous isotonic vehicle. A range from 0.7 to 1.2% of Sodium Chloride solution equivalent is acceptable.

The normal range of tears pH is from 7.0 to 8.5. Not only does this vary from person to person but there is also a daily temporal variation within the same individual. For this reason a solution may show a pH range from 6.0 to 8.5 with greater initial comfort and nearer to the physiological average of 7.2.

**Protein Removing Compounds**

One reason for removing contact lens deposits is to extend the useful life of the lens. However, more important reasons for cleaning lenses are to maintain clear vision, good comfort and most importantly normal eye health.

Proteins are a major source of soft contact lens contamination. Proteins and related moieties have been implicated in bacterial adhesion to contact lenses and proteins have been blamed for a variety of problems and adverse reactions experienced by contact lens wearers such as giant papillary conjunctivitis (GPC).
There are many commercially available cleaning regimens for removing protein deposits from hydrophilic contact lenses. Investigations into the effectiveness of different cleaning solutions have been largely non differential and have used simple and subjective methodologies based to a great extent on visual observations. For remaining proteins, enzymatic and non enzymatic cleaning systems are used. The purpose of both enzymatic and non enzymatic is to reduce/ remove deposits. However enzymes themselves are proteins and therefore have potential to bind to the surface of the contact lens. Some bind to the lens more than others. This can increase the potential for irritation and discomfort.

According to the literature and market survey Papain based tablets have the greatest amount of enzyme uptake onto the lens. Although allergic reactions are less in Papain treatment than Pancreatin. Non enzymatic cleaners like subtilisin buffers are preferred since they offer many advantages over enzymatic cleaners (26, 64, 140).

Protein removal compounds are an important part of contact lens care. The purpose of enzymatic and non enzymatic cleaning is not disinfection but removal of contact lens debris. Enzymes act by directly attacking substrates (protein, lipid and mucin) and catalyzing their breakdown into smaller molecular units which are more easily removed by mechanical action such as rubbing and rinsing. Contact lens wearers prone to allergies should not use enzymes but non enzymatic multipurpose solution. Non enzymes cleaners are non allergic and act by chelating like Citrates, Phosphates, Tris buffer and Hydranate.

All contact lenses, particularly soft lenses, absorb/adsorb surface deposits. FDA Group IV high water, ionic soft lenses also absorb/adsorb proteins (primarily lysozyme) into the internal lens matrix. These lenses have a shorter useful life than lenses made from other polymers. Group IV soft lenses in use today are frequently manufactured as disposable lenses with replacement recommended after two weeks of wear. Loosely absorbed surface deposits on these and all lenses should be removed at the end of the day by mechanically rubbing the lens in the palm of the hand using a surfactant cleaner or all-in-one solution. Enzymatic cleaning on a daily or weekly basis removes the majority of proteins which have become ionically bound to the lens surface. Absorbed deposits in the matrix of soft contact lenses may partially be removed by overnight soaking in solutions containing surfactant cleaners.
Hydranate is hydroxyalkylphosphonate and is tetravalent anionic protein cleaning agent which has recently been introduced but it is a TM chemical used by Bausch & Lomb. It is a sequestering agent and chelating compound.

The second generation multipurpose solution therefore consist of drug (antimicrobial agent /preservative), sequestering and chelating agent, buffering agent, tonicity agent, lubricating agent, viscosity imparting agent and protein removing agent in a sterile base.