Electrodeionization in Pharmaceutical Water Treatment

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Electrodeionization is a technology that uses ion-exchange resin sheets and beads as well as electrical potential to remove undesirable contaminants from pretreated feed water. A significant advantage to using this technology in place of conventional mixed-bed ion-exchange technology is the elimination of the need for on-site regeneration chemicals.

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Water treatment in the pharmaceutical industry commonly involves highly developed technologies such as reverse osmosis (RO), ultrafiltration, UV irradiation, ion exchange (IX), and distillation. Electrodeionization (EDI) is a cost-effective water treatment method that is becoming increasingly standard. This article describes how and why the procedure is implemented in pharmaceutical water treatment plants.

Compendial waters

Pharmaceutical water treatment plants typically remove sufficient contaminants from treated municipal drinking water to meet *USP* standards required for compendial waters. The term *compendial waters* represents any water intended to be used for final drug dosage forms, including sterile purified water (PW), sterile water for injection, sterile bacteriostatic water for injection, sterile water for irrigation, and sterile water for inhalation.

Sterile purified water and certain sterile water for inhalation products are made with PW that is processed in a pharmaceutical water treatment plant. For PW, *USP* guidelines require a conductivity limit of 0.6–4.7 μS/cm, a total organic carbon or total oxidizable carbon (TOC) limit of 500 ppb (μg/L), and a bacteria-count limit of 100 cfu/mL. The conductivity limit is determined by a three-stage process that accounts for the temperature and pH of the water.

Sterile water for injection, sterile bacteriostatic water for injection, sterile water for irrigation, and certain sterile water for inhalation products, collectively referred to as *water for injection* (WFI), are produced from water processed in a pharmaceutical water treatment plant. For WFI, the USP guidelines require a conductivity limit of 0.6–4.7 μS/cm that is determined by the same three-stage process as for PW; a TOC limit of 500 ppb (μg/L); an endotoxin limit of 0.25 endotoxin units/mL; and a bacteria-count limit of 10 cfu/100 mL.

Distillation

The principal difference between PW and WFI is the allowable amount of bacterial contamination, which is measured by colony count and by endotoxin level. Endotoxins are pieces of cell wall from certain bacteria. Most water treatment plants ensure the control of the bacterial count in WFI by instituting a

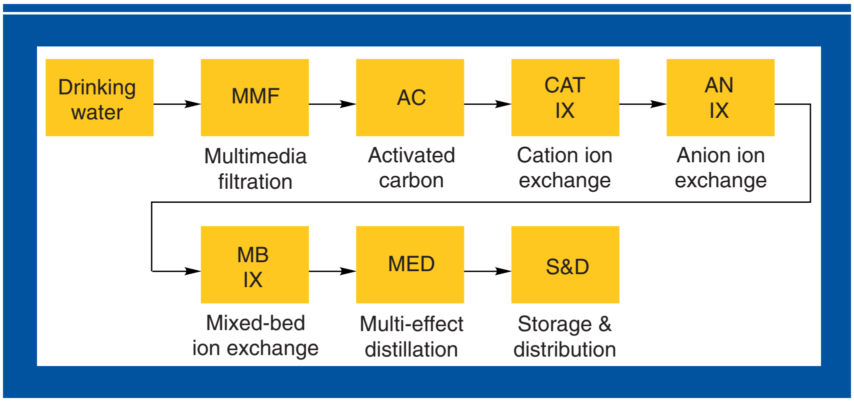

Figure 1: An example of pre–membrane water treatment methods.

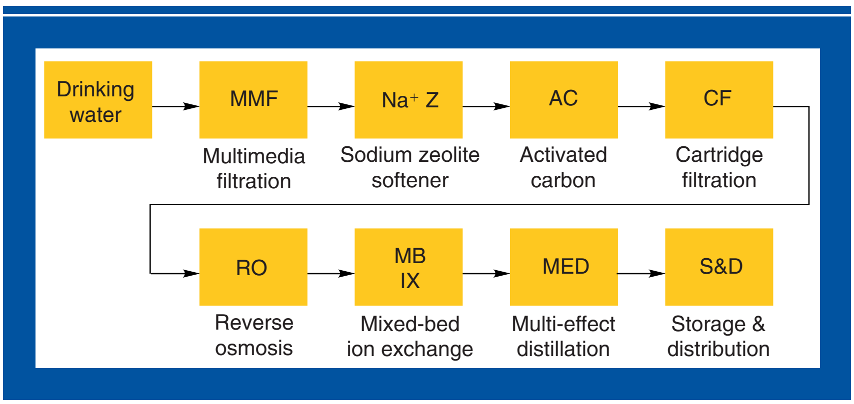

Figure 2: A representation of a typical RO water treatment system.

distillation unit called a *still* as the final treatment step before storage and distribution. The high temperatures and liquid-to-vapor phase change in a still generally ensure that a distillate will meet bacterial contamination limits. Two types of stills commonly are used: vapor compression (VC) and multi-effect (ME). A VC still may require only a softener and an activated-carbon bed as pretreatment. An ME still requires high-quality feed water. EDI commonly is used in conjunction with an ME still in pharmaceutical water treatment systems.

Pre–membrane water treatment methods

To understand why EDI currently is regarded so favorably, it is helpful to consider pharmaceutical water treatment methods of the past. Figure 1 shows an example of pre–membrane water treatment methods. In the past, *membrane water treatment* generally meant RO membrane water treatment. Presently, membrane water treatment includes microfiltration, ultrafiltration, nanofiltration, hyperfiltration (i.e., RO), EDI, and electrodialysis.

Every water treatment plant is unique. Figure 1 does not represent a standard but is merely an example to illustrate some of the subsystems of a pre–membrane water treatment system. The purpose of each subsystem is described briefly in this section.

Multimedia filtration. Multimedia filters are designed to remove the bulk of suspended contaminants whose size exceeds 10–30 μm. As a reference, the diameter of a human hair measures roughly 100 μm.

Activated carbon (AC). AC beds, also known as *activated carbon filters,* most commonly are used to remove chlorine and chloramine compounds from feed water. This filtration process protects downstream equipment such as RO membranes and IX resin beads from the damaging oxidizing action of chlorine and chloramine compounds.

IX units. IX technology exchanges undesirable feed water cations and anions with desirable cations and anions. Cations are positively charged atoms and molecules. Anions are negatively charged atoms and molecules. Cation IX units exchange undesirable feed water cations such as calcium, magnesium, lead, and copper with desirable hydrogen ions (H^+). Anion IX units exchange undesirable feed water anions such as chloride, sulfate, phosphate, and nitrate with desirable hydroxide ions (OH^-). The resulting H^+ and OH^- ions then combine to form water.

To further purify water, mixed-bed IX units often are placed after cation and anion units. A mixed-bed unit has both cation and anion resin beads that are thoroughly mixed together. The water exiting a mixed-bed IX unit usually is polished to the extent that it meets USP conductivity limits for both PW and WFI.

Distillation. Distillation units heat the feed water to its boiling point. Most dissolved and suspended contaminants remain in the water phase. The steam that is produced is condensed and typically meets WFI and PW standards.

RO water treatment

RO water treatment has become the standard at many pharmaceutical water treatment plants. RO technology can be a cost-effective replacement for dual cation and anion IX units. Figure 2 illustrates the RO treatment process.

Cation IX units must be regenerated with a strong acid—either sulfuric, which is generally used, or hydrochloric. Anion IX units must be regenerated with a strong base, usually sodium hydroxide, which is also referred to as *caustic* or as *caustic soda.* Daily regeneration may be necessary. RO systems are desirable because they reduce the need to use costly chemicals, especially those that are caustic, and they curtail the ever-increasing cost of regeneration waste disposal. The payback that results from using an RO system can be achieved in less than two years in some situations.

An RO membrane system can remove as much as 98–99% or more of all dissolved contaminants and can remove essentially all suspended (particulate) contaminants. However, RO units require pretreatment to prevent scaling, fouling with living and nonliving particulate materials, and chemical attack, commonly by oxidizing agents. Figure 2 shows the pretreatment steps in a typical RO system.

Softening. A softener is a type of IX technology that controls scaling in downstream equipment. A softener controls scaling

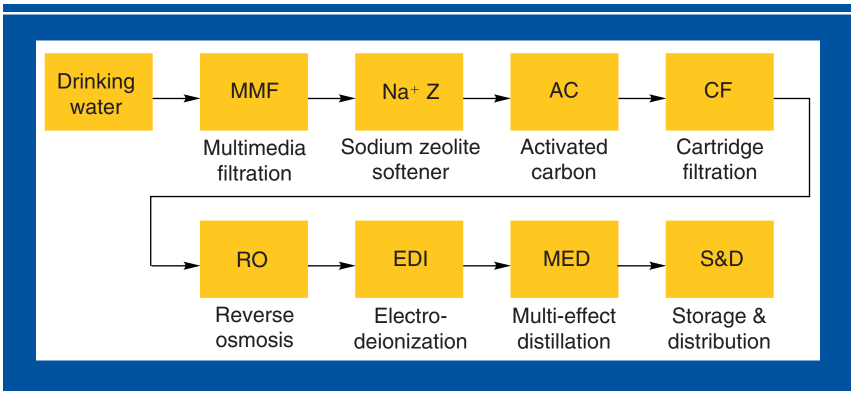

Figure 3: An EDI unit can cost-effectively replace mixed-bed IX units.

by removing hard scale–forming cations such as calcium and magnesium and exchanging (i.e., replacing) these ions for non-scale-forming sodium ions. An older term, *sodium zeolite softening*, frequently is used to describe water softening.

Cartridge filtration. Cartridge filtration or other prefiltration technology is used ahead of RO units to protect against fouling from suspended particles in the feed water. RO membrane systems may become fouled if sufficient suspended solids (particulate) removal is not accomplished. Typically, 1–5-µm nominally rated filter cartridges are used.

Mixed-bed IX units usually are positioned after an RO subsystem. The effluent from a mixed-bed IX unit meets *USP* conductivity limits for PW and WFI. UV irradiation may be used for bacterial control. The effluent from the mixed-bed IX unit in the example shown in Figure 2 feeds an ME still that produces WFI distillate for storage and distribution.

EDI water treatment

For essentially the same reason that cation and anion units are cost-effectively replaced by RO units, EDI units in many cases can cost-effectively replace mixed-bed IX units. Figure 3 shows an example in which EDI has been applied for this purpose. The resin beads in EDI units do not require chemical regeneration by acid and caustic. EDI units are continuously regenerated electrically.

Figure 4 shows a typical EDI unit that comprises alternating sheets of cation and anion resin, somewhat analogous to a plate-and-frame heat exchanger. A spacer is located between each pair of resin sheets to provide a channel between them. Every other channel is filled with cation and anion resin beads that are thoroughly mixed together, similar to those in a mixed-bed IX unit. Every other channel not filled with cation and anion resin beads is a brine channel (i.e., concentrate or waste stream). The total collection of alternating resin sheets, spacers, and resin beads is called a *stack*.

On either end of a stack is an electrode. When direct current is applied to the electrodes, the electrode at one end of the stack

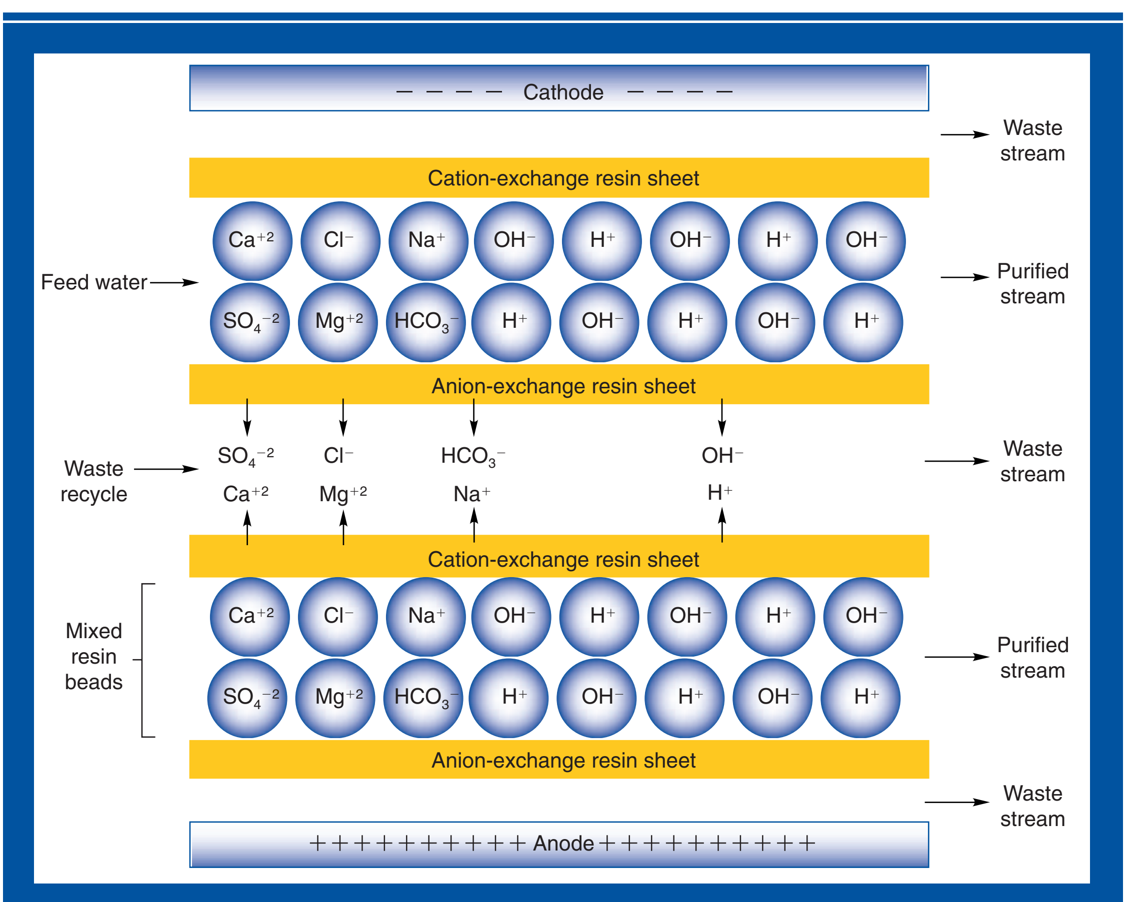

Figure 4: The composition of a typical EDI unit.

is positively charged (anode) and attracts negatively charged anions. The other end of the stack is negatively charged (cathode) and attracts positively charged cations.

Feed water cations entering an EDI stack eventually are exchanged for H^+ ions, and feed water anions eventually are exchanged for OH^- ions. Together, the H^+ and OH^- ions form water. The undesirable feed water cations in the resin beads migrate through a cation-exchange resin sheet toward the cathode. The undesirable feed water anions in the resin beads migrate through an anion-exchange resin sheet toward the anode. Once a cation or anion has passed through one resin sheet, it cannot pass through the next sheet. Feed water cations can pass only through cation resin sheets, and feed water anions can pass only through anion resin sheets. Therefore, the undesirable feed water ions are trapped within a brine channel and carried away.

The electrical potential applied to the stack also can split water molecules into H^+ and OH^- ions. Because cation resin beads normally are regenerated with H^+ ions and anion beads normally are regenerated with OH^- ions, the beads are regenerated continuously while the unit is operating.

The effluent from many EDI subsystems meets *USP* conductivity requirements for PW and WFI. If the effluent is destined to be used as PW, then UV irradiation may be implemented for bacterial control. Feeding the EDI effluent to an ME still is a commonly used technique in the production of WFI.

Summary

PW and WFI, which are used in the production of various drugs, are required to meet conductivity, TOC, and bacteria-count limits. In addition, WFI must meet the *USP* endotoxin limit. Generally, several treatment steps use various water treatment technologies to produce PW or WFI from drinking-water-quality feed water. To reduce or eliminate the cost and hazard of regenerating acid and caustic and the cost of regeneration waste disposal, treatment plants can be incorporated with RO units that can cost-effectively replace cation and anion exchange units. For essentially the same reasons, EDI units in many cases can cost-effectively replace mixed-bed IX units. **PT**

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