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Remington: The Science and Practice of Pharmacy

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Remington: The Science and Practice of Pharmacy . . . *A treatise on the theory and practice of the pharmaceutical sciences, with essential information about pharmaceutical and medicinal agents; also, a guide to the professional responsibilities of the pharmacist as the drug information specialist of the health team . . . A textbook and reference work for pharmacists, physicians, and other practitioners of the pharmaceutical and medical sciences.*

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PHILADELPHIA COLLEGE OF PHARMACY AND SCIENCE

A juice is prepared from fresh ripe fruit, is aqueous in character, and is used in making syrups that are employed as vehicles. The freshly expressed juice is preserved with benzoic acid and allowed to stand at room temperature for several days, until the pectins that naturally are present are destroyed by enzymatic action, as indicated by the filtered juice yielding a clear solution with alcohol. Pectins, if allowed to remain, would cause precipitation in the final syrup.

Cherry Juice (RPS-18 page 1320) is described in the USP XXI and Raspberry Juice in USP XVIII. Concentrated Raspberry Juice (PC, 11th ed) is prepared from the clarified juice of raspberries. Pectinase is stirred into pulped raspberries and the mixture allowed to stand for 12 hours. The pulp is pressed, the juice clarified, and sufficient sucrose added to adjust the weight at 20° to 1.050 to 1.060 g per mL. The juice then is concentrated to one-sixth of its original volume. Sufficient sulfurous acid or sodium metabisulfite is added as a preservative.

Artificial flavors now have replaced many of the natural fruit juices. Although they lack the flavor of the natural juice, they are more stable and easier to incorporate into the final pharmaceutical form. Commercial juices such as orange, apple, grape, and mixed vegetables have been used recently to prepare extemporaneous preparations of cholestyramine and nizatidine.

Information on cranberry juice indicates that it may be effective in controlling some urinary tract infections and urolithiasis.

NASAL SOLUTIONS

Nasal solutions are usually aqueous solutions designed to be administered to the nasal passages in drops or sprays. Other nasal preparations may be in the form of emulsions or suspensions. Although many of the drugs are administered for their local sympathomimetic effect—such as Ephedrine Sulfate or Naphazoline Hydrochloride Nasal Solution USP, to reduce nasal congestion—a few other official preparations, Lypressin Nasal Solution USP and Oxytocin Nasal Solution USP, are administered in spray form for their systemic effect for the treatment of diabetes insipidus and *milk letdown* prior to breast feeding, respectively. The current route of administration of peptides and proteins is limited to parenteral injection because of inactivation within the gastrointestinal tract. As a result, there is considerable research on intranasal delivery of some of these drugs such as analogs of enkephalins or luteinizing-hormone–releasing hormone and insulin. Other drugs that are absorbed poorly from the GI tract, such as gentamicin sulfate, are being administered in the form of nasal solutions to obtain appropriate blood levels. Some pharmaceuticals such as meperidine HCl and lidocaine HCl may be administered in the form of nasal solutions for analgesia and headaches, respectively.

Nasal solutions are prepared so that they are similar in many respects to nasal secretions in regard to toxicity, pH, and viscosity so that normal ciliary action is maintained. Thus, the aqueous nasal solutions usually are isotonic and slightly buffered to maintain a pH of 5.5 to 6.5. In addition, antimicrobial preservatives, similar to those used in ophthalmic prepara-

mainly in the atrium and cleared slowly into the pharynx wi
the patient in an upright position. Drops spread more exte
sively than the spray, and three drops cover most of the wa
of the nasal cavity with the patient in a supine position a
head tilted back and turned left and right. It is suggested th
drop delivery, with appropriate movement by the patient, lea
to extensive coverage of the walls of the nasal cavity.

OTIC SOLUTIONS

These solutions occasionally are referred to as aural prepar
tions. Other otic preparations often include formulations su
as suspensions and ointments for topical application in the e

The main classes of drugs used for topical administration
the ear include analgesics, such as benzocaine; antibiotics, su
as neomycin; and anti-inflammatory agents, such as cortisor
The USP preparations include Antipyrine and Benzocaine O
Solution. The Neomycin and Polymyxin B Sulfates and Hydr
cortisone Otic Solutions may contain appropriate buffers, s
vents, and dispersants usually in an aqueous solution. T
main solvents used in these preparations include glycerin
water. The viscous glycerin vehicle permits the drug to rema
in the ear for a long time. Anhydrous glycerin, being hygr
scopic, tends to remove moisture from surrounding tissue
thus reducing swelling. Viscous liquids like glycerin or pr
pylene glycol are used either alone or in combination with
surfactant to aid in the removal of cerumen (ear wax). Sodiu
Bicarbonate Ear-Drops BP may be used if wax is to be remov
from the ear. This preparation contains sodium bicarbonate
g), glycerin (30 mL), and purified water (a sufficient quantity
make 100 mL).

To provide sufficient time for aqueous preparations to act,
is necessary for patients to remain on their side for a fe
minutes so the drops do not run out of the ear. Otic prepar
tions are dispensed in a container that permits the admin
tration of drops.

IRRIGATION SOLUTIONS

Irrigation solutions are used to wash or bathe surgical in
sions, wounds, or body tissues. Because they come in conta
with exposed tissue, they must meet stringent requirements
the USP such as sterility, total solids, and bacterial endotoxin
These products may be prepared by dissolving the active ingr
dient in Water for Injection. They are packaged in single-do
containers, preferably Type I or Type II glass, or suitable pla
tic containers, and then sterilized. See Chapter 40 for steriliz
tion procedures. A number of irrigations are described in th
USP, eg, Acetic Acid Irrigation for bladder irrigation, Dimeth
Sulfoxide Irrigation for relief of internal cystitis, Neomycin an
Polymyxin B Sulfates Solution for Irrigation for infection, an
Sodium Chloride Irrigation for washing wounds.

Extemporaneous formulations frequently are prepared u
ing an isotonic solution of sodium chloride as the solvent. F
example, cefazolin or gentamicin in 0.9% sodium chloride a
used as anti-infective irrigations, dinoprostone in lactated rin

segment of the globe and to affect the nerves and other structures in that space.

PREPARATION

The preparation of ophthalmic solutions, suspensions, or ointments by the community pharmacist or even the hospital pharmacist is becoming less common. The pharmacist may be called upon to prepare a special concentration, particularly of an antibiotic, in the hospital setting. However, the extemporaneous compounding of ophthalmic prescriptions is becoming rare. In those cases when the pharmacist is called upon to compound an ophthalmic preparation extemporaneously, careful documentation along with physician consultation is required. Meticulous attention to detail and the use of a detailed, preapproved preparation plan must be in place prior to compounding.[11] In the view of many, the advantages of commercial preparations, such as stability, uniformity, and sterility, outweigh possible disadvantages such as standardization of dosage. A general discussion concerning the preparation of ophthalmic solutions is found in USP 23, which lists 59 items.

VEHICLES—Sterile isotonic solutions, properly preserved, are suitable for preparing ophthalmic solutions (see Chapter 18). In most cases, when the concentration of active ingredient is low, ie, less than 2.5 to 3.0%, the drug can be dissolved directly in the isotonic vehicle. The finished solutions will be hypertonic somewhat but well within the comfort tolerance of the eye.

Typical stock solutions are as follows:

Isotonic Sodium Chloride Solution

Sodium Chloride USP	0.9 g
1:10,000	Benzalkonium Chloride
Sterile Distilled Water	qs 100 mL

Boric Acid Solution

Boric Acid USP	1.9 g
1:10,000	Benzalkonium Chloride
Sterile Distilled Water	qs 100 mL

Boric acid solution at pH 5 is an appropriate vehicle for the following:

Cocaine	Procaine
Neostigmine	Tetracaine
Phenacaine	Zinc salts
Piperocaine	

Boric acid solution with an antioxidant is useful for oxygen-sensitive drugs such as epinephrine, phenylephrine, or physostigmine. The following solutions are suggested. Phenylmercuric nitrate replaces benzalkonium chloride as the preservative in the first solution.

Boric Acid	1.9 g
Sodium Sulfite Anhydrous	0.1 g
Phenylmercuric nitrate	1:50,000
Sterile Purified Water	qs 100 mL
Sodium Acid Phosphate (NaH_2PO_4) anhydrous	0.56 g
Disodium Phosphate (Na_2HPO_4) anhydrous	0.284 g
Sodium Chloride	0.5 g
Disodium Edetate	0.1 g
Benzalkonium Chloride	1:10,000
Sterile Purified Water	qs 100 mL

These vehicles are suitable for salts of

Atropine	Homatropine
Ephedrine	Pilocarpine

STERILIZATION PROCEDURES—Those procedures suited best for the extemporaneous preparation of ophthalmic solutions are

1. Solutions in final container
   a. Place the filtered solution in containers that have been washed and rinsed with distilled water.
   b. Seal dropper bottles with regular screwcaps. The dropper assembly should be stapled into a paper envelope.
   c. Sterilize 20 min at 15 psi (121°).
   d. Do not assemble until ready to use.
2. Dropper bottles
   a. Wash container thoroughly and rinse with distilled water.
   b. Loosen caps and place bottles in autoclave.
   c. Autoclave 15 min at 15 psi (121°).
   d. Partially cool autoclave.
   e. Remove bottles from autoclave and secure caps.
   f. Store sterilized bottles in a clean, dustproof cabinet.
3. Glassware and equipment
   a. Wrap adapters (containing filter), syringes, glassware, spatulas, etc, in autoclave paper and secure with masking tape.
   b. Place articles in autoclave and sterilize in the manner described in Section 2 above.
   c. Store in separate cabinet until ready to use.
4. Microbiological filtration
   a. All equipment and glassware as well as stock solutions should be sterile. The prescription should be dispensed in a sterile container.
   b. Unwrap sterile syringe and draw prepared solution into syringe.
   c. Unwrap sterile adapter containing bacterial filter and attach to syringe. These are available as single-filtration, presterilized, disposable units and should be used whenever possible.
   d. Force solution through filter directly into sterile container (dropper or plastic *Drop-Tainer* (Alcon) type).
   e. By employing an automatic filling outfit, more than one container of the same prescription can be prepared.
   f. Cap container immediately.

The procedures outlined above should be carried out in a clean area equipped with ultraviolet lighting and preferably in a laminar-flow hood.

Laminar-Flow Principles—A laminar-flow work area is a particularly convenient means of preparing sterile, particulate-free solutions. Laminar flow is defined as air flow in which the total body of air moves with uniform velocity along parallel lines with a minimum of eddies. Laminar flow minimizes the possibility of airborne microbial contamination by providing air free of viable particles and free of practically all inert particulates. Laminar-flow units are available in a variety of shapes and sizes and in two broad categories, horizontal and vertical laminar flow. It should be noted that laminar flow *per se* is not a guarantee of sterility. Correct procedures and sterile techniques remain necessary. See Chapter 40.

General Considerations

A number of requirements must be considered in the preparation of ophthalmic solutions, suspensions, or ointments. These include sterility, clarity, buffer, buffer capacity and pH, tonicity, viscosity, stability, comfort, additives, particle size, packaging, and preservatives. Many of these requirements are interrelated and must be considered collectively in the preparation of an ophthalmic product. The buffer system must be considered with tonicity and comfort in mind. Stability can

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