Pharmaceutical and Clinical Calculations

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Calculations Involving Topical Ophthalmic, Nasal, and Otic Preparations

A variety of pharmaceutical dosage forms are applied topically to the eye, nose, and ear which include solutions, suspensions, and ointments. In general, drugs are applied to the eye for the local effects of the medication, either on the surface of the eye or its interior. Amongst the various types of dosage forms for the eye, aqueous solutions are the most frequently used. In the extemporaneous preparation of ophthalmic formulations, one should consider sterility, preservation, isotonicity, pH and buffering, and viscosity. Nasal preparations are generally used for their decongestant activity on the nasal mucosa. Important considerations in the preparation of nasal solutions include isotonicity, pH and buffering, and viscosity. Ear preparations are also referred to as *otic* or *aural* preparations. Most of the official ear preparations are aqueous solutions of medications. They are used for treating mild infections, softening wax, cleansing after infections, drying wet surfaces, and as antiseptics. The important considerations in the formulation of otic products include pH and buffering. For example, an otic product with a pH value of less than 4 may cause burning and stinging sensation in the ear canal.

The present chapter deals with calculations involving isotonicity, pH, and buffering of topical preparations. The discussion presented here is also relevant to the dosage forms for other routes of administration including parenteral routes.

ISOTONICITY

Whenever a solution is separated from a solvent by a membrane permeable only to solvent molecules but impermeable to solutes (referred to as a "semipermeable membrane''), the solvent passes across the membrane into the solution. This is the phenomenon of osmosis, which may be defined as the passage of solvent molecules across a semipermeable membrane against the concentration gradient. Osmosis can also occur when a concentrated solution is separated from a less concentrated solution by a semipermeable membrane. The pressure differential that develops across the membrane is called ''osmotic pressure.''

Osmotic pressure is a colligative property and is dependent on the number of particles of solute(s) in a solution. The total number of particles of a solute in a solution is the sum of the undissociated molecules and the number of ions into which the molecule dissociates. The number of ions, in turn, depends on the degree of ionization. Thus, a chemical that is highly ionized contributes a greater number of particles to the solution than the same amount of a poorly ionized chemical. When a chemical is a nonelectrolyte such as sucrose or urea, the concentration of the solution depends only on the number of molecules present. The values of the osmotic pressure and other colligative properties are approximately the same for equal concentrations of different nonelectrolyte solutions.

Body fluids, including blood and tears, have the same osmotic pressure as that of a 0.9% w/v sodium chloride solution. Solutions having the same osmotic pressure as that of 0.9% w/v NaCl solution are said to be *isotonic* with blood. Solutions with a higher osmotic pressure than body fluids are called *hypertonic* and those with a lower osmotic pressure are called *hypotonic*.

Osmotic effects are very important from a physiological standpoint. This is because biological membranes including the membrane of red blood cells behave like semipermeable membranes. Consequently, when red blood cells are immersed in a hypertonic solution (e.g., D_5 ½ NS or D_5NS), they shrink as water leaves the blood cells in an attempt to dilute and establish a concentration equilibrium across the blood cell membrane. Thus, when hypertonic solutions are administered into the blood stream, the fluid moves from interstitial and cellular space into the intravascular space. Conversely, when cells are placed in hypotonic environment (e.g., ½ NS), they swell because of the entry of fluid from the intravascular compartment, and may eventually undergo lysis.

In the eye, hypertonic solutions may cause drawing of water towards the site of application; whereas hypotonic solutions may cause water to move from the topical application site through the tissues of the eye. When instilled into the eye, isotonic solutions cause no contraction or swelling of the tissues with which they come in contact, and cause no discomfort. Therefore, it is very important to adjust the isotonicity of topical ophthalmic products. Isotonic adjustments are also important for nasal and aural preparations, parenteral products, and irrigating solutions. In a given product, all the

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