



Buffers in Compounding Pharmacies

A Practical Guide for Pharmacists

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Buffers play a critical role in the formulation of compounded medications. In the context of compounding pharmacies, buffers help stabilize the pH of a solution, ensuring that the active pharmaceutical ingredients (APIs) maintain their efficacy, solubility, and stability. For pharmacists working in compounding pharmacies, understanding the mechanisms and proper use of buffers is essential to optimizing both patient outcomes and the quality of compounded medications.

What Are Buffers?

Buffers are aqueous solutions that resist changes in pH when small amounts of acids or bases are added. In pharmaceutical compounding, buffers usually consist of a weak acid and its conjugate base, or a weak base and its conjugate acid. These systems are particularly important in maintaining the pH within an optimal range for the stability and effectiveness of APIs.

Why Buffers Matter in Compounding

The role of buffers in pharmacy compounding cannot be overstated. The pH of a formulation directly affects:

1. **Stability:** Many APIs are sensitive to pH, and an incorrect pH level can lead to degradation or precipitation. By using an appropriate buffer, pharmacists can prolong the stability of a medication.
2. **Solubility:** The solubility of an API is often pH dependent. For example, weakly acidic drugs are more soluble in basic environments, while weakly basic drugs are more soluble in acidic environments.

Buffer systems allow pharmacists to maintain the desired solubility throughout the medication's shelf life.

3. **Patient Comfort:** For routes of administration such as ophthalmic, nasal, or injectable preparations, maintaining a pH close to physiological conditions (e.g., pH 7.4) is essential to minimize irritation and enhance patient comfort.

Common Buffer Systems Used in Pharmaceutical Preparations

Compounding pharmacists utilize a variety of buffer systems, depending on the route of administration and the required pH range of the formulation. Some commonly used buffer systems include:

- **Citrate Buffer:** Effective in pH ranges from 2.5 to 6.5, the citrate buffer is frequently used in both internal and external formulations.
- **Phosphate Buffer:** This is one of the most versatile buffers, working within a pH range of 6.0 to 8.0. It is often employed in ophthalmic, nasal, and parenteral preparations to maintain a pH close to physiological levels.
- **Acetate Buffer:** Suitable for both internal and external use, the acetate buffer operates within a pH range of 3.6 to 5.6, making it ideal for formulations that need to maintain mild acidity.
- **Sodium Bicarbonate Buffer:** This buffer is effective for both internal and external use and works in the pH range of 8.0 to 9.0. It is commonly used in formulations where alkalinity is required for stability or solubility, such as in certain injectable preparations.

Practical Considerations for Buffer Use in Compounding

1. **Buffer Capacity:** The buffer capacity determines the buffer's ability to resist pH changes upon the addition of acids or bases. It is important to ensure that the buffer capacity is high enough to maintain stability without altering the therapeutic properties of the formulation.
2. **Compatibility with APIs:** Some buffer systems may interact with APIs or excipients, affecting their solubility or stability. For instance, certain APIs may degrade in the presence of specific salts or acids used in buffers. Pharmacists must assess compatibility during formulation.
3. **Route of Administration:** The choice of a buffer is also influenced by the intended route of administration. For instance, ophthalmic solutions require isotonicity and a pH close to tears (pH ~ 7.0-7.4) to minimize discomfort, while injectable solutions must be both isotonic and close to the physiological pH of blood (pH ~ 7.35-7.45).
4. **Regulatory Guidelines:** Pharmacists must adhere to established guidelines, such as those set by the United States Pharmacopeia (USP), when selecting and using buffers in compounded medications.

Challenges in Buffer Selection and Use

While buffers are critical for maintaining pH stability, pharmacists must navigate some challenges during their selection and application:

- **Formulation Volume:** The buffer must be carefully calculated so that it does not significantly increase the volume of the formulation, particularly in injectable or ophthalmic preparations where precise dosing is critical.
- **Irritation Potential:** While buffers help maintain pH balance, their components (e.g., phosphate or citrate salts) can cause irritation if not correctly balanced, especially in sensitive areas like the eyes or nasal mucosa.
- **Preservatives:** Some buffers require the addition of preservatives to maintain sterility in multi-dose formulations. However, preservatives themselves can affect the pH and overall stability, requiring careful consideration during formulation.

Practical tips: maximum buffer concentrations by route

Different buffers have specific characteristics that make them more or less suitable for different applications. Here's a brief overview based on common practice:

1. **Injectable Routes:** For injectable formulations, achieving a pH close to physiological levels (pH 7.35-7.45) is critical to avoid irritation or pain. Phosphate buffers are often preferred for this route because they can be used in slightly higher concentrations (typically up to 50 mM) without causing significant discomfort. Citrate buffers, on the other hand, tend to cause more pain at higher concentrations, so they are typically limited to lower concentrations, often under 10 mM, for injectable formulations.
2. **Ophthalmic Solutions:** Buffers used in ophthalmic formulations need to maintain both a pH close to 7.0-7.4 and isotonicity to ensure comfort. Phosphate buffers are commonly used here as well, typically at concentrations of 5-50 mM. Higher concentrations can increase the risk of irritation, especially with sensitive tissues like the eyes.
3. **Nasal Preparations:** For nasal formulations, maintaining a pH close to physiological levels while minimizing irritation is important (typically in the range of pH 5.5-7.0, with a target around pH 6.5). Both phosphate and acetate buffers are used, but concentrations tend to be on the lower side to minimize irritation. Citrate buffers are again used more cautiously because of their potential to cause discomfort at higher concentrations.
4. **Oral and Topical Applications:** Oral and topical formulations often have more flexibility in terms of buffer concentration. Acetate and phosphate buffers are commonly used here, with concentrations ranging from 10-100 mM depending on the desired pH and the formulation's characteristics. Since these routes don't have the same discomfort concerns as injectables or ophthalmic preparations, buffer concentration is often guided more by the stability and solubility requirements of the active pharmaceutical ingredients (APIs).

Conclusion

Buffers are essential in compounding pharmacy, ensuring that formulations remain stable, effective, and comfortable for patients. By understanding the role of different buffer systems and their practical applications, pharmacists can enhance the quality and performance of their compounded medications.

Whether compounding for oral, topical, injectable, or ophthalmic routes, pharmacists should select buffers that are compatible with the API and suited to the intended route of administration. Proper buffer selection ensures that medications meet both therapeutic and safety standards, contributing to better patient outcomes.

Reference:

1. Ferreira, A., Polonini, H., Brandão, M.A. Guia Prático da Farmácia Magistral, 6th ed., 2023.

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